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ON CHLORIMIDOQUINONES

BY LEMUEL CHARLES RAIFORD

In 1890 Hantzsch and Werner[1] formulated the theory that the isomerism of nitrogen compounds of the same composition and structure which contain a doubly bound nitrogen atom is of the same nature as the stereoisomeric ethylene derivatives, like maleic and fumaric acids. In accordance with the theory we should have the two configurations

$$\begin{matrix} X—C—Y \\ \| \\ Z—N \end{matrix} \qquad \text{and} \qquad \begin{matrix} X—C—Y \\ \| \\ N—Z \end{matrix}$$

The objections of Victor Meyer[2] that the differences between the isomeric benziloximes amd dioximes might depend on peculiarities of the hydroxylamine molecule were met by Hantzsch[3] by the preparation of stereoisomeric phenylhydrazones of anisylphenylketone; but he was unable to extend[4] the proof beyond these two closely related groups of compounds, the oximes and the hydrazones, his efforts to prepare stereoisomers in which Z in the above formula is represented by such simple radicals as CH_3, C_6H_5, etc., being un-

[1] Ber. d. chem. Ges., **23**, 11 and 1243 (1890).
[2] *Ibid.*, **16**, 503 (1883); **21**, 784, 3510 (1888).
[3] *Ibid.*, **24**, 3525 (1891).
[4] Hantzsch: "Stereochemie," p. 141.

successful. The first representatives of such stereoisomers, other than oximes and hydrazones, were prepared in 1903 by Stieglitz znd Earle[1] in the form of a pair of stereoisomeric chlorimido esters in which Z in the configuration given is represented by a single chlorine atom. Stieglitz and Hale[2] prepared a second pair of stereoisomers in 1904, and Hilpert,[3] working with Stieglitz in 1907, added five pairs of such compounds to the list. The type is now characterized on a broad and firm basis.[4]

In order to investigate the question of the occurrence of stereoisomeric chlorimides in classes of compounds other than the acid esters, Professor Stieglitz suggested to me to determine whether stereoisomerism can be observed in the case of chlorimidoquinones, comparable with that of the quinone oximes, discussed and investigated by Kehrmann.[5] Although six chlorimidoquinones whose structure would admit of the occurrence of such stereoisomerism were prepared and studied, and though the structure was varied to cover all the possible types, instances of stereoisomerism were not observed, not even in the case of the chlorimide of 2-chlor-5-methylquinone, whose oxime, according to Kehrmann,[6] has the most favorable structure for the occurrence and persistence of this form of stereoisomerism. Stieglitz and Hale found that the labile form of stereoisomeric chlorimidonitrobenzoates is very readily converted into the stable form by the action of chlorine and Hilpert confirmed this observation for the chlorimido esters which he studied. Whether the failure to obtain stereoisomeric chlorimidoquinones is due to the fact that chlorine was present in the solution in which the chlorimides were prepared, and that the method of preparation[7] necessarily involved a much greater time of contact of the reagents with the material than in the case of the preparation of the chlor-

[1] THIS JOURNAL, **30**, 399 (1903); **40**, 37 (1908).

[2] Unpublished reports.

[3] THIS JOURNAL, **40**, 150 (1908).

[4] Stereoisomeric chlorimido ketones have recently been prepared by Stieglitz and Peterson.

[5] Ann. Chem. (Liebig), **279**, 27 (1894); **303**, 1 (1898).

[6] *Loc. cit.*

[7] The oxidation of *p*-aminophenols with hypochlorous acid in acid solution.

imido esters, or whether one of the two possible forms is so much the more stable that it is obtained exclusively, it is impossible, of course, to say. It is quite a common experience that cases of stereoisomerism theoretically possible are not readily realizable by our preparation methods.

In the study of the chlorimidoquinones for this work a number of interesting new observations were made on compounds of the phenol and quinone series, and, in particular, some incorrect statements and uncertain points given in the literature on the preparation and structure of such compounds were noted and corrected. All our conclusions were carefully verified by experimental work. In the following paper the most interesting of the observations made are reported.

I. 4-Chlorimido-2-bromquinone

The starting point in the preparation of this compound was 4-nitrophenol, which was first brominated according to the method of Brunk[1] and Körner.[2] The resulting brom compound was purified by crystallization of its barium salt, from which, by subsequent treatment with hydrochloric acid, the free phenol was obtained. The latter was finally crystallized from water, from which it separated out in colorless needles that melt at 112°.[3] It was further identified by the preparation of its reduction products, the corresponding amine and its hydrochloride.

Hydrochloride of 2-Brom-4-aminophenol.—2-Brom-4-nitrophenol was dissolved in the smallest possible quantity of hot alcohol (1 gram to 1 cc.) and to the hot solution was added one-fourth more than the calculated amount of stannous chloride, dissolved in concentrated hydrochloric acid (1 gram to 1 cc.). During this time the flask was shaken and the mixture kept hot in order to prevent the immediate separation of crystals. Next, one volume of concentrated hydrochloric acid was added and the solution set aside to cool. Crystals of the amino hydrochloride soon separated

[1] Z. Chem., **1867**, 204.

[2] *Ibid.*, **1868**, 323.

[3] The statement of Brunk that 2-brom-4-nitrophenol melts at 102° is probably a misprint. Meldola and Streatfield (J. Chem. Soc., **73**, 681 (1898)) prepared this compound by nitrating *o*-bromphenol, and they found 112° as the melting point.

out. These were filtered off and recrystallized as follows: The crude material was dissolved in warm water and the solution filtered through paper, after which one volume of concentrated hydrochloric acid was added to the filtrate. Upon standing, slightly yellowish crystals of the amino hydrochloride, free from tin compounds, were deposited.

The hydrochloride thus obtained is readily soluble in water containing a trace of acid, in alcohol, and in a solution of sodium hydroxide. When heated to 225° the compound begins to blacken, but does not melt. A sample dried *in vacuo* over potassium hydroxide for 72 hours was analyzed for halogen and gave the following results:

0.2913 gram substance gave 0.4311 gram AgHal.

	Calculated for $C_6H_7ONClBr$	Found
Halogen	51.42	51.56

2-Brom-4-aminophenol.—The free amine was easily obtained by treatment of a water solution of the hydrochloride described above with ammonium carbonate solution. The precipitated amine was filtered off at once, and dried on a clay plate. In this condition it melted at 164° and was very nearly pure. The compound is soluble in alcohol, chloroform, ether, and a solution of sodium hydroxide, but much less soluble in benzene. It is best crystallized from the last-named liquid, from which it separates in needles having a faintly brownish color and melting at 165°. Analysis for bromine gave the following figures:

0.2450 gram substance gave 0.2474 gram AgBr.

	Calculated for C_6H_4ONBr	Found
Br	42.54	42.97

4-Chlorimido-2-bromquinone, $O : C_6H_3Br : NCl$.—A portion of the hydrochloride of 2-brom-4-aminophenol, weighing 5 grams, was dissolved in 75 cc. of water to which a trace of hydrochloric acid had been added, and the resulting solution cooled to about 0°. This liquid was then allowed to flow slowly from a tap funnel into acidulated (hydrochloric acid) solu-

tion of sodium hypochlorite[1] which had been cooled to 0°, and in which pieces of ice were floating. The flask containing the hypochlorite was kept surrounded by a mixture of ice and water, and was shaken continuously while the amino hydrochloride was being added. A yellow solid, having the characteristic odor of a chlorimidoquinone, was promptly precipitated, and after standing for a few minutes was filtered off and washed several times with cold water.

When dried on a clay plate the chlorimide began to darken after 24 hours, a change that goes on more rapidly as the temperature rises. The crude product did not have a characteristic melting point, but decomposed suddenly, after softening, when heated above 60°. The compound is soluble in alcohol, ether and chloroform, but less readily so in ligroin. It is best crystallized from the low-boiling (40°–60°) fraction of the latter liquid, because the heat required to saturate the higher boiling fractions to a sufficient degree to give a satisfactory yield of crystals will decompose the chlorimide. Attempts to fractionate[2] the compound gave negative results. The purest product obtainable decomposed, without melting, when heated to 60°, as already indicated.

For analysis, the method employed by Stieglitz and Earle[3] in the determination of halogen in their chlorimido esters, consisting in the liberation of iodine from hydrogen iodide, was first tried; but concordant results could not be obtained, because not only the chlorimide group but the quinone ring, too, oxidizes the hydrogen iodide. Halogen was determined, in this and all other compounds described in this paper, by the Carius method.

0.3460 gram substance gave 0.5233 gram AgHal.

	Calculated for $C_6H_3ONClBr$	Found
Halogen	52.36	52.71

II. 4-Chlorimido-2-chlor-6-bromquinone

This chlorimidoquinone was prepared in accordance with

[1] Graebe: Ber. d. chem. Ges., **35**, 43 and 2753 (1902).
[2] Hilpert: *Loc. cit.*
[3] THIS JOURNAL, **30**, 402 (1903).

the method already described. The starting point was 2-chlor-6-brom-4-nitrophenol, melting at 137°, which was obtained by brominating 2-chlor-4-nitrophenol in glacial acetic acid solution.[1] A portion of this nitro compound was converted into the corresponding amino hydrochloride[2] by reduction with stannous chloride in the manner already described. By recrystallization of the product colorless plates, that blackened and decomposed without melting when heated above 225°, were obtained. Analysis for halogen gave the following figures:

0.2614 gram substance gave 0.4789 gram AgHal.

	Calculated for $C_6H_6ONCl_2Br$	Found
Halogen	58.27	58.26

2-Chlor-6-brom-4-aminophenol.[3]—The free amine was readily obtained from a water solution of the hydrochloride by precipitation with ammonium carbonate. The mixture was at once filtered and the residue well washed with water, and dried on a clay plate. In this condition the substance is but slightly colored and is otherwise practically pure. It is soluble in alcohol, ether, chloroform, benzene, and a solution of sodium hydroxide. It is best crystallized from benzene, from which it separates in colorless, thin, elongated scales having a melting point of 181°. Analysis for halogen gave the following figures:

0.2411 gram substance gave 0.3606 gram AgHal.

	Calculated for $C_6H_5ONClBr$	Found
Halogen	51.88	52.13

4-Chlorimido-2-chlor-6-bromquinone, $O : C_6H_2BrCl : NCl$.—When a cold solution of the hydrochloride of 2-chlor-6-brom-4-aminophenol was dropped slowly into a cold solution of sodium hypochlorite in the usual way, a yellow solid having the odor characteristic of a chlorimidoquinone was formed.

[1] Ling: J. Chem. Soc., **55**, 57 (1889). Clark: THIS JOURNAL, **14**, 563 (1892).

[2] Clark (*loc. cit.*) found that this hydrochloride forms a double salt with tin chloride, but he did not isolate the hydrochloride of the amine.

[3] This compound is probably identical with Clark's product, though he reports neither melting point nor analysis.

The mixture was filtered, and the solid washed well with cold water and dried on a clay plate. In this condition it melted at 83°–84°. Attempts to fractionate it gave portions of material having the same melting point. The chlorimide is soluble in alcohol, ether, chloroform and ligroin. After being crystallized from ligroin (70°–80°), it melted at 87°–88°, and decomposed suddenly, with charring, when heated to about 175°. The crystals darken after a few days when kept under ordinary conditions. Analysis for halogen gave the results indicated below:

0.2770 gram substance gave 0.5143 gram AgHal.

	Calculated for $C_6H_2ONCl_2Br$	Found
Halogen	59.19	59.02

The study of a dihalogenated chlorimidotoluquinone was next suggested, and an effort was made to obtain this by means of 2,4,6-trichlor-*m*-cresol. It was hoped that this could be nitrated in such a way as to replace by the nitro group the chlorine atom in the para position to the hydroxyl group. In the parallel case of 2,4,6-tribrom-*m*-cresol such substitution takes place very readily, as observed by Claus and Hirsch.[1] No difficulty was experienced in preparing trichlor-*m*-cresol—statements in the literature to the contrary notwithstanding—but it was then found impossible to effect the desired substitution, the trichloride being very much less reactive than the tribromide.

2,4,6-Trichlor-m-*cresol.*[2]—In a study of the action of chlorine on the cresols, Claus and Schweitzer[3] found that *m*-cresol gave a dichlor compound, and that more chlorine could not be introduced. Chandelon[4] studied the action of chlorinating agents on phenol, and found that treatment of an aqueous solution of phenol with a solution of sodium hypochlorite at 60°–70° gave trichlorphenol. After repeating Chandelon's work and obtaining the same results, I

[1] J. prakt. Chem., [2] **39**, 61 (1888).

[2] The trichlortoluenol prepared by Lallemand (Jahresb., **1886**, 620) and reported by Beilstein as trichlorcresol, can hardly be identical with this compound.

[3] Ber. d. chem. Ges., **19**, 929 (1886).

[4] Bull. soc. chim., **38**, 116 (1882).

tried the method with *m*-cresol. An impure product was at first obtained, but the greater portion of it turned out to be the desired compound, 2,4,6-trichlor-*m*-cresol. When the operation was carried out at room temperature instead of 60°–70°, as in the first case, a much better yield of a purer product was secured. This was further purified by distillation in an Anschütz flask. The larger fraction came over at 142°–144° and 14 mm. as an oil which, upon cooling, crystallized out in the form of colorless plates melting at 47°.

Trichlor-*m*-cresol is but slightly soluble in water, but is readily soluble in a solution of sodium hydroxide, from which it is completely precipitated by carbon dioxide. Alcohol, ether, chloroform and ligroin dissolve it easily. Its saturated aqueous solution is not colored violet by ferric chloride. It was analyzed for chlorine and gave the following results:

0.1849 gram substance gave 0.3773 gram AgCl.

	Calculated for $C_7H_5OCl_3$	Found
Cl	50.31	50.40

2,4,6-Trichlor-3-methylphenyl Acetate.—A portion (5 grams) of trichlor-*m*-cresol was mixed with anhydrous sodium acetate and slightly more than the theoretically required amount of acetic anhydride. Action began at once, causing considerable rise of temperature. The flask was warmed until the contents were fluid, and it was then allowed to remain on the electric heater in this condition for about ten minutes. When the solid that formed upon cooling was mixed with water, in order to remove sodium acetate, the acetyl derivative separated out as an oil, which was further washed with water, dried over calcium chloride and distilled. At 273°–274° the chief portion came over as a colorless, viscid liquid of about the consistence of glycerol. The compound was analyzed for chlorine and gave the following figures:

0.2107 gram substance gave 0.3578 gram AgCl.

	Calculated for $C_9H_7O_2Cl_3$	Found
Cl	41.97	42.00

Several attempts were next made to nitrate 2,4,6-trichlor-*m*-cresol. When a glacial acetic acid solution of the compound was mixed with solid sodium nitrite,[1] in accordance with Zincke's method, the unchanged trichlorcresol was recovered from the mixture. Shaking its ethereal solution with silver nitrite also gave negative results. Fuming nitric acid at the room temperature converts it into 2,6-dichlortoluquinone, along with resinous products.

2,6-Dichlortoluquinone.—Further proof of the structure of 2,4,6-trichlor-*m*-cresol was obtained by oxidizing a portion of it to quinone, which was done by the aid of dichromate mixture. Five grams of trichlor-*m*-cresol was dissolved in 150 cc. glacial acetic acid, and the solution cooled to about 0°, and to this was added gradually the cold dichromate solution. This mixture was allowed to stand for half an hour, after which it was diluted with one volume of water. The yellow solid that formed subsided during an hour, and was then filtered off, washed well with water, and dried on clay plate. A yield of 72 per cent. was obtained.

This quinone is soluble in chloroform, ether, ligroin, and alcohol. Portions crystallized from ligroin and alcohol, respectively, melted at 103°, which agrees with the results obtained by Claus and Schweitzer,[2] when they oxidized dichlor-*m*-cresol. My product is also probably identical with the dichlortoluquinone prepared by Southworth[3] from *m*-cresol, though he states that he could obtain no melting point for his compound, as it began to sublime at 100°. The substance obtained from trichlor-*m*-cresol was shown, both by analysis and by the depression of its melting point when mixed with 4-chlortoluquinone (melting at 105°), not to be an impure sample of the latter. The mixture melted between 85° and 95°. Analysis for chlorine resulted as follows:

0.2242 gram substance gave 0.3380 gram AgCl.

	Calculated for $C_7H_4O_2Cl_2$	Found
Cl	37.14	37.24

[1] J. prakt. Chem., [2] **61**, 561 (1900).
[2] Ber. d. chem. Ges., **19**, 931 (1886).
[3] Ann. Chem. (Liebig), **188**, 270 (1873).

2,6-Dichlortoluhydroquinone.—The dichlortoluquinone (2.5 grams) was mixed with 60 cc. water and the mixture saturated with sulphur dioxide. After standing overnight the mixture was heated to the boiling point, enough water gradually added to dissolve the solid, and then the solution was filtered through paper and set aside to cool. The needle-shaped crystals that formed were collected and dissolved in hot water and the solution saturated with sulphur dioxide. The colorless needles that crystallized out melted at 171°, as found by Claus and Schweitzer,[1] and in close agreement with the results of Southworth.[1]

After being dried *in vacuo* over potassium hydroxide for 24 hours the hydroquinone was analyzed for chlorine.

0.3531 gram substance gave 0.5244 gram AgCl.

	Calculated for $C_7H_6O_2Cl_2$	Found
Cl	36.76	36.70

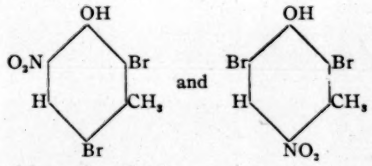
III. 4-Chlorimido-2,6-dibromtoluquinone

The starting point in the preparation of this compound was pure *m*-cresol, obtained by fractionating Kahlbaum's product. From this material 2,4,6-tribrom-*m*-cresol was prepared in accordance with Werner's method.[2]

Pure tribrom-*m*-cresol obtained as above specified was next nitrated.[3] Thirty grams of the compound was dissolved in 300 cc. glacial acetic acid, the liquid cooled to 12°–15° and then 10 per cent. more than the calculated quantity of sodium nitrite added during half an hour, while the flask was continually shaken and the temperature kept down to that given above. When the nitrite had all dissolved, the dark liquid was poured with stirring into five volumes of water, and the mixture set aside for some hours to allow the precipitate to subside. At the end of this time the yellow solid was filtered off and dried on a clay plate. A yield of 95 per cent. was obtained. The crude product softened at 65° and

[1] *Loc. cit.*
[2] Bull. soc. chim., **46**, 275 (1886).
[3] Zincke: J. prakt. chem., [2] **61**, 561 (1900).

was completely melted at 113° (when it appeared to decompose), which suggested the possible presence of two compounds.[1] It may be stated at once that isomeric mononitrodibrom-*m*-cresols, viz.,



were isolated from the mixture.

The best method of separating the compounds present was found to consist in dissolving the dried crude product in hot chloroform (1 gram to 1 cc.) and treating this solution with two volumes of ligroin (40°–60°). Precipitation of the high-melting isomer (para compound) took place at once. After half an hour this was filterd off and crystallized from benzene, when a compound melting at 128°, with decomposition,[2] was secured. Repeated crystallization from the same solvent finally gave pale yellow plates melting at 134° with decomposition.[3] The substance so obtained has the nitro group in the para position as respects hydroxyl, and is 2,6-dibrom-4-nitro-*m*-cresol. A yield of 35 per cent. was obtained.

When the filtrate from the chloroform-ligroin mixture specified above was allowed to evaporate, it left a yellowish red, sticky mass which, after repeated crystallizations from alcohol, gave deep yellow needles melting at 87°.[4] This compound is isomeric with the nitro product mentioned above, and was proved (see below) to have the nitro group adjacent to hydroxyl. A yield of 40 per cent. was obtained.

[1] A mixture of the isomers, purified as described in this paper, melts at 79°–115° with decomposition. Zincke reported the formation of only one isomer, in which the bromine atom para to the hydroxyl group had been replaced.

[2] Zincke: J. prakt. Chem., [2] **61**, 563 (1900).

[3] Claus: *Ibid.*, [2] **39**, 61 (1888).

[4] Claus (*loc. cit.*) prepared this compound by brominating 6-nitro-*m*-cresol, and found 93° to be the melting point.

In view of the fact that the melting points found for these compounds did not agree with those given by other workers, both substances were analyzed for halogen and several of their derivatives prepared and studied. Analyses of the nitro compounds for bromine gave the following figures:

I. The para compound, 2,6-dibrom-4-nitro-*m*-cresol.
0.4668 gram substance gave 0.5662 gram AgBr.

	Calculated for $C_7H_5O_3NBr_2$	Found
Br	51.43	51.26

II. The ortho compound, 2,4-dibrom-6-nitro-*m*-cresol.
0.4266 gram substance gave 0.5156 gram AgBr.

	Calculated for $C_7H_5O_3NBr_2$	Found
Br	51.43	51.42

Hydrochloride of 2,6-Dibrom-4-amino-m-*cresol.*—Five grams of the *p*-nitro compound was dissolved in 20 cc. hot alcohol, and to this solution was added stannous chloride dissolved in concentrated hydrochloric acid, as before specified. The hydrochloride obtained upon cooling was recrystallized in the manner already described, and gave colorless needles free from tin compounds. The crystals are readily soluble in water containing a trace of hydrochloric acid, in a solution of sodium hydroxide (giving a liquid that at once becomes brown), and in alcohol, and almost insoluble in chloroform. When heated above 225° the substance blackens but does not melt.

2,6-Dibrom-4-amino-m-*cresol.*—The free amine was easily prepared from the hydrochloride by treatment of an aqueous solution of the latter with ammonium carbonate. The precipitated base, after being filtered off, washed well with water and dried on a clay plate, melted at 175°–176° with blackening.[1] It is readily soluble in alcohol, benzene, chloroform and a solution of sodium hydroxide, less soluble in ligroin and practically insoluble in water. Portions of the com-

[1] Zincke's statement (J. prakt. Chem., [2] **61**, 564 (1900)) that this compound melts at 116° is possibly a misprint, or he had the *o*-amino compound in his hands. He appears to have overlooked the formation of this substance, which melts at 116°, as given below.

pound purified by crystallization from alcohol and by treatment of a chloroform solution with an equal volume of ligroin (40°–60°), respectively, in both of which cases it separated in colorless crystals, melted at 176°. It was analyzed for nitrogen.

I. 0.4905 gram substance gave 0.0236 gram N (Kjeldahl).
II. 0.4925 gram substance gave 0.0238 gram N.

	Calculated for $C_7H_7ONBr_2$	Found I	Found II
N	4.98	4.81	4.83

2,6-Dibrom-4-benzoylamino-m-*cresol.*—In order to further identify the amine, a portion of it was benzoylated in accordance with the Baumann method, using 2.5 molecules of benzoyl chloride. The product was found to be soluble in alcohol, chloroform and benzene, less soluble in ligroin, and insoluble in water. It was best purified by treatment of its hot chloroform solution with one volume of ligroin (40°–60°), when colorless crystals melting at 198° were obtained. The pure compound was soluble in a solution of sodium hydroxide and from this hydrochloric acid precipitated the original substance. These results indicated a monobenzoylated product, and they were confirmed by an analysis for nitrogen.

0.4550 gram substance gave 0.0165 gram N (Kjeldahl).

	Calculated for $C_{14}H_{11}O_2NBr_2$	Found
N	3.63	3.62

3,5-Dibrom-6-methyl-p-*hydroxyphenylurethane,* $HOC_6HBr_2(CH_3)NHCO_2C_2H_5$.—The first efforts to prepare this compound were made in accordance with Groenvik's[1] method, but the yield was very small and the product could not easily be purified. A much purer substance in satisfactory yield was secured by shaking an alkaline solution of 2,6-dibrom-4-amino-*m*-cresol (obtained by dissolving the amine in a solution of sodium hydroxide) with one molecule of ethyl chlorcarbonate for about ten minutes and, after al-

[1] Bull. soc. chim., **25**, 177 (1876).

lowing the mixture to stand for half an hour, acidifying it with dilute hydrochloric acid. The substance thus obtained was found to be soluble in a solution of sodium hydroxide, from which acids precipitated it in the unchanged form. It was easily purified by mixing with its warm chloroform solution two volumes of ligroin (40°–60°) and removing the brownish solid that was precipitated at once. The urethane melts sharply at 155°, and after being dried for 24 hours *in vacuo* gave the following results when analyzed for nitrogen.

I. 0.6198 gram substance gave 0.0224 gram N (Kjeldahl).
II. 0.5752 gram substance gave 0.0217 gram N.

	Calculated for $C_{10}H_{11}O_2NBr_2$	Found I	Found II
N	3.96	3.63	3.77

Up to this point the derivatives prepared and analyzed indicate that the amine under consideration has the formula assigned to it. The relative positions of the amino and the hydroxyl groups were determined by the behavior of the compound when oxidized with the usual dichromate mixture, in which case it gave a quinone melting at 117°, and evidently identical with the 2,6-dibromtoluquinone that Claus and Dreher[1] obtained by oxidizing 2,4,6-tribrom-*m*-cresol. In order to decide this a portion of the tribrom-*m*-cresol used in the preparation of the compounds described above was oxidized to quinone in accordance with the directions given by Claus. A compound having a melting point of 117°, which was not depressed when mixed with the quinone obtained directly from the amine, resulted.

4-Chlorimido-2,6-dibromtoluquinone, $O : C_6HBr_2(CH_3) : NCl$. —When a cold solution of the hydrochloride of 2,6-dibrom-4-amino-*m*-cresol was oxidized in the usual way with an acidified solution of sodium hypochlorite, an immediate precipitate of chlorimidoquinone was formed. This was filtered off

[1] J. prakt. Chem., [2] **39**, 370 (1889). Claus and Dreher found that this dibromtoluquinone melts at 115°. Claus and Hirsch (*Ibid.*, p. 60) report 117° as the melting point of the corresponding hydroquinone; but this is probably an error, since hydroquinones usually melt much higher than their quinones. Reduction of our dibromtoluquinone with sulphur dioxide in the usual way gave a hydroquinone that crystallized from water in colorless crystals and had a constant melting point of 150°.

and washed with water, and when dried on a clay plate it melted at 85°–86°. A yield of 85 per cent. was obtained. The compound is readily soluble in alcohol, chloroform, and ligroin, but insoluble in water. Attempts to fractionate the substance in accordance with the methods indicated above gave crystals having the same melting point, 86°. The best method of purification of the chlorimide is crystallization from ligroin (40°–60°), from which it separates in yellow hexagonal plates melting at 86°, and having the characteristic odor of this class of substances. Determination of nitrogen resulted as follows:

I. 0.5990 gram substance gave 0.0263 gram N (Kjeldahl).
II. 0.7515 gram substance gave 0.0334 gram N.

	Calculated for $C_7H_4ONClBr_2$	Found	
N	4.46	4.39	4.44

It has been noted (p. 427) that the nitration of 2,4,6-tribrom-*m*-cresol under the conditions described in this paper gives rise to two isomeric mononitro derivatives, one of which (melting at 134° with decomposition) has been shown to have the nitro group para to hydroxyl. When this had been done it was at once suspected that the other one (melting at 87°) had the nitro group ortho to hydroxyl. The behavior of its derivatives described below shows that this is the case.

Hydrochloride of 2,4-Dibrom-6-amino-m-*cresol.*—Five grams of 2,4-dibrom-6-nitro-*m*-cresol was dissolved in 50 cc. hot alcohol and then reduced with stannous chloride in the usual way. It was noted that the hydrochloride obtained is much less readily soluble in water than is its isomer, the para compound, and could not be purified in exactly the manner employed with the latter. Two modifications were tried, viz., crystallization from alcohol and treatment of the alcoholic solution with concentrated hydrochloric acid. In both cases the crystals secured were free from tin compounds. Exactly as in the case of the para compound, this hydrochloride is but sparingly soluble in chloroform, but is readily soluble

in a solution of sodium hydroxide, forming a brown liquid. Nitrogen determinations gave the following figures:

I. 0.6942 gram substance gave 0.0292 gram N (Kjeldahl).
II. 0.5553 gram substance gave 0.0239 gram N.

	Calculated for $C_7H_5ONClBr_2$	Found I	Found II
N	4.41	4.20	4.30

2,4-Dibrom-6-amino-m-*cresol.*—A solution of the hydrochloride in very dilute hydrochloric acid was mixed with a slight excess of a solution of ammonium carbonate, and the precipitated amine at once filtered off and washed well with water. When dry the base was further purified by treatment of its warm chloroform solution with two volumes ligroin (40°—60°), from which it crystallized in brownish scales melting at 116–°117°.[1] Alcohol, chloroform and solutions of sodium hydroxide dissolve the amine easily, giving in the latter case a strongly colored liquid. Nitrogen analyses gave the results recorded below:

I. 0.6323 gram substance gave 0.0326 gram N (Kjeldahl).
II. 0.6683 gram substance gave 0.0342 gram N.

	Calculated for $C_7H_7ONBr_2$	Found I	Found II
N	4.98	5.15	5.11

2,4-Dibrom-3-methyl-6-benzoylaminophenyl Benzoate. — The amine just described was further identified by treatment with benzoyl chloride by the Baumann method, 2.5 molecules of benzoyl chloride being used. The product was collected on a filter, dried on a clay plate, and repeatedly crystallized from alcohol until it was practically colorless and melted sharply at 188°. The compound is easily soluble in chloroform and ether, less readily so in ligroin, and insoluble in solutions of sodium hydroxide. It was regarded as the dibenzoylated compound, and analysis for nitrogen agreed with this view:

[1] It will be noted that Zincke (J. prakt. Chem., [2] **61**, 564 (1900)) found 116° as the melting point of the para compound, while I found 176° for the compound that I proved to be the para product.

I. 0.5070 gram substance gave 0.0156 gram N (Kjeldahl).
II. 0.5070 gram substance gave 0.0159 gram N.

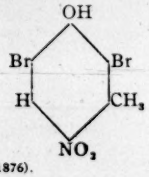
	Calculated for $C_7H_{15}O_2NBr_2$	Found I	Found II
N	2.86	3.07	3.13

3,5-Dibrom-4-methyl-o-hydroxyphenylurethane, $HOC_6H(CH_3)$-$Br_2NHCO_2C_2H_5$.—As in the case of the para compound, an attempt was made to prepare this urethane by Groenvik's method[1], but the very small yield, taken in connection with the difficulty experienced in obtaining a pure product, made it advisable to try some other method. A yield of 60 per cent. was obtained by shaking an alkaline solution of the corresponding aminocresol with one molecule of ethyl chlorcarbonate, and the product was not difficult to purify. It was crystallized by miximg with its warm chloroform solution an equal volume of ligroin (40°–60°). The crystals that separated were brownish and readily soluble in alcohol and in solutions of sodium hydroxide, from which liquid they were separated unchanged by the addition of acid. They melted sharply at 169°. A portion of the compound dried *in vacuo* for 24 hours was analyzed for nitrogen.

I. 0.6776 gram substance gave 0.0271 gram N (Kjeldahl).
II. 0.5376 gram substance gave 0.0201 gram N.

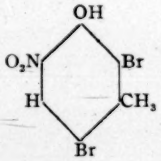
	Calculated for $C_{10}H_{11}O_3NBr_2$	Found I	Found II
N	3.96	3.99	3.73

The preparation and analyses of the derivatives of the dibromnitro-*m*-cresol now under consideration indicate that it is isomeric with the one already disposed of, and which was shown to have the structure



[1] Bull. soc. chim., 25, 177 (1876).

by the ease with which it was ultimately converted into the corresponding quinone. Direct proof that the substance now in question has the nitro group adjacent to hydroxyl, and has the structure



was secured as follows:

In a study of the behavior of aminophenols, Ladenburg[1] found that he could distinguish between the ortho and para varieties by the difference in reaction of the two compounds toward acetic anhydride. The ortho compounds give condensation products which he called ethenylaminophenols, or anhydro bases,

$$O—C_6H_4—N = C—CH_3$$

while the para compounds give diacetyl derivatives,

$$CH_3CO.O.C_6H_4NHCOCH_3.$$

This method was tried on the aminocresol obtained from the nitro compound now being studied.

2,4-Dibrom-3-methyl-6-acetylaminophenyl Acetate. — Three grams of the corresponding dibromamino-*m*-cresol was mixed with acetic anhydride (2 mol.) as above indicated. Interaction began immediately with the evolution of heat. The flask was next attached to a reflux condenser and warmed gently until the mass became liquid, after which it was boiled for two hours. Upon cooling, a solid that melted at 207° was formed. Repeated crystallization from alcohol gave long, colorless, silky needles melting sharply at 216°, soluble in chloroform and ligroin, but insoluble in solutions of sodium hydroxide except on standing. The behavior toward alkali

[1] Ber. d. chem. Ges., **9**, 1524 (1876).

pointed to a diacetyl derivative, and this indication was confirmed by analyses for nitrogen and bromine.

I. 0.4134 gram substance gave 0.0165 gram N (Kjeldahl). 0.2382 gram substance gave 0.2466 gram AgBr.

II. 0.3711 gram substance gave 0.0144 gram N.

	Calculated for $C_{11}H_{11}O_3NBr_2$	Found I	Found II
N	3.83	3.99	3.88
Br	43.82	44.08	....

That the base is nevertheless an *o*-aminophenol derivative is shown conclusively by the following determination. In a study of the rearrangements of *o*-aminophenylethyl carbonate, Ransom,[1] working with Stieglitz, showed that when its hydrochloride is dissolved in water it goes over into *o*-hydroxyphenylurethane. Upson,[2] also working with Stieglitz, studied this rearrangement in quite a number of substances, and found that while it is a general reaction for ortho compounds it does not take place with the corresponding para compounds. With these facts in view, tle dibromnitro-*m*-cresol (melting at 87°) in question was converted into its carbonate, and this was reduced to the amino hydrochloride, and the latter then allowed to react with water in the usual way. Its behavior showed conclusively that the dibromnitro-*m*-cresol (melting at 87°) is an *o*-nitrophenol, and that its reduction product is an *o*-aminophenol.

2,4-Dibrom-3-methyl-6-nitrophenylethyl Carbonate, $O_2NC_6HBr_2(CH_3)OCO_2C_2H_5$.—Six grams of 2,4-dibrom-6-nitro-*m*-cresol was dissolved in 300 cc. water containing slightly more than the theoretically required amount of sodium hydroxide, and to this was added 1.25 molecules of ethyl chlorcarbonate, after which the mixture was shaken for twenty to thirty minutes, or until the red color characteristic of the sodium salt of the nitrocresol had disappeared. A yellow oil, that solidified on cooling, separated out, and after standing for some time was filtered and dried. The substance is very soluble in alcohol, ether, chloroform, ligroin and glacial acetic acid, and

[1] THIS JOURNAL, **23**, 43 (1900).
[2] *Ibid.*, **25**, 13 (1904).

could not be crystallized from any of these liquids. The purest sample secured was obtained by pouring the glacial acetic acid solution into water. The oil that separated solidified on standing, and was then filtered off and dried. It melted at 43°–45°.

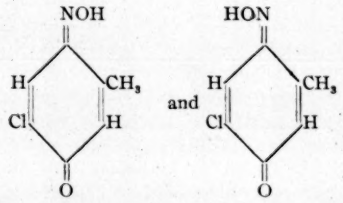
The nitrocarbonate was next reduced[1] by shaking its glacial acetic acid solution with tin[2] and concentrated hydrochloric acid until the liquid was practically colorless, after which it was filtered through paper and the filtrate mixed with two volumes of water and then allowed to stand overnight in order to enable the phenolcarbonate to rearrange and form the corresponding urethane by a migration of the carbonate group from the phenol group to the amine group.[3] The solid that formed was collected on a filter and dried on a clay plate. In this condition it melted at 167°–169°. It was further purified by solution in warm chloroform and treatment of this solution with one volume of ligroin (60°–80°). The crystals so obtained melted sharply at 169°, which is the melting point of 3,5-dibrom-4-methyl-*o*-hydroxyphenylurethane already described (p. 433). A mixture of these two products has the same melting point as either of them separately, from which it follows that they are identical, and that in the dibromnitro-*m*-cresol in question the hydroxyl and the nitro groups are adjacent to each other. It will be noted that this method of proving the relative positions of the hydroxyl and nitro (amino) groups by means of rearrangement is easier of execution and gives more conclusive evidence than does Ladenburg's method.

IV. The Three Chlorimidochlortoluquinones

In their proof of the structure of the stereoisomeric oximes obtained from 4-chlortoluquinone, Kehrmann and Tichvinsky[4] found that reduction of the oximes by means of stannous chloride gave a chloraminocresol that is identical with the base they obtained when they reduced the product secured

[1] Ransom: THIS JOURNAL, **23**, 14 (1900).
[2] Equally satisfactory results were obtained by the use of zinc.
[3] Ransom: *Loc. cit.*
[4] Ann. Chem. (Liebig), **308**, 20 (1898).

by chlorinating 6-nitro-*m*-cresol in glacial acetic acid solution. In the latter reaction Kehrmann[1] assumed that chlorine took a position para to methyl, and from such a view assigned to the oximes the stereoisomeric formulas



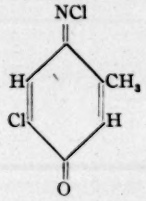
He states that this is the structure most favorable to the occurrence and persistence of this form of stereoisomerism. My experiments in the attempts to prepare the stereoisomeric chlorimidoquinones corresponding to these oximes involved the preparation of a chloraminocresol from 6-nitro-*m*-cresol, and it was found to have a melting point of 166°–167°, which is different from that (204°–205°) given by Kehrmann, a fact that at once made necessary a repetition of Kehrmann's work on the oximes. The latter were prepared (the stereoisomers were not separated) and reduced according to the directions given, and the resulting hydrochloride of the chloraminocresol decomposed by ammonium carbonate in the usual way. The base obtained melted at 206°–207°, which is in close agreement with the observation of Kehrmann. The acetyl derivative, the quinone and the hydroquinone obtained from this base also had the properties reported by Kehrmann and others[2] in the literature. It was further identified by the preparation of its dibenzoate (p. 444).

When the chloraminocresol (melting at 206°–207°) was oxidized to the chlorimidoquinone it gave a product melting at 91°, while the chloraminocresol (melting at 166°–167°)

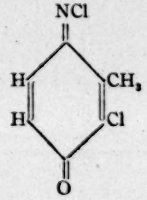
[1] *Loc. cit.*

[2] Schniter's statement (Ber. d. chem. Ges., **20**, 2286 (1887)) that the monochlorinated toluquinone, melting at 105°, could not be obtained free from the higher chlorinated products is not confirmed by the analysis reported by him. The calculated percentage of chlorine given by him is incorrect.

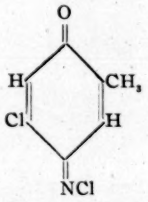
obtained from the chlorine derivative of *p*-nitro-*m*-cresol gave a chlorimidoquinone melting at 87°. A mixture of the two chlorimides melts at 65°–70°, which shows that they are not identical. If Kehrmann's assumptions as to the structure of the chlornitro-*m*-cresol formed by chlorinating *p*-nitro-*m*-cresol were correct, the two chlorimides would have the same structure and would therefore be stereoisomers of the type sought by us. However, the low melting point obtained by me for the chloraminocresol prepared by way of chlornitro-*m*-cresol, as compared with the melting point (204°–205°) given by Kehrmann for the chloraminocresol obtained by reduction of his oximes (and confirmed by me) suggested plainly that the two chlorimides, as well as the two amino products, might well be structural isomers rather than stereo-isomers. By subsequent investigation I was able to prove that the chlorimides are indeed structural isomers—the chlor-imide, melting at 91°, obtained from Kehrmann's chloramino-cresol having the structure of 6-chlorimido-4-chlortoluquinone,



while that obtained from the chloraminocresol, melting at 166°–167°, derived from *p*-nitro-*m*-cresol of is 6-chlorimido-2-chlortoluquinone,



melting at 87°. A third chlorimidochlortoluquinone, melting at 65°, was obtained from 2-methyl-4-amino-5-chlor-*o*-cresol (from *m*-nitro-*p*-chlortoluene) and has the structure of 4-chlorimido-2 methyl-5-chlorquinone,

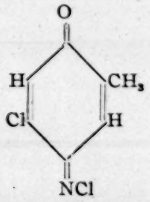


6-Chlorimido-4-chlortoluquinone.—It is possible that when Kehrmann chlorinated *p*-nitro-*m*-cresol, the chlorine, to a certain extent at least, entered the position para to the methyl group, in the way he assumed (Kehrmann did not isolate the chloride); but when I carried out the chlorination of the same substance, following Kehrmann's directions as closely as the brief descriptions will permit, except that I isolated and purified all my products, the chlorine, as proved below, must have persistently entered chiefly into the position ortho to the methyl group, that is, between it and the hydroxyl group. It seems possible, now that I have cleared up the facts, that in both cases a mixture of both chlorides is formed—the proportions varying according to conditions that have not yet been determined; and that Kehrmann obtained derivatives (amine, etc.) of one compound, while I secured those of another. It is beyond question, however, that the derivative which I isolated is always formed under the conditions followed by me. In a very closely related case, the chlorination of *o*-nitrotoluene, I was able to establish conclusively (see below) the formation of the two chlorine derivatives, containing chlorine ortho and para to the methyl group, although Janson[1] had reported the formation of but one (in this case the ortho compound).

[1] Centralb., **1900**, I. 1110.

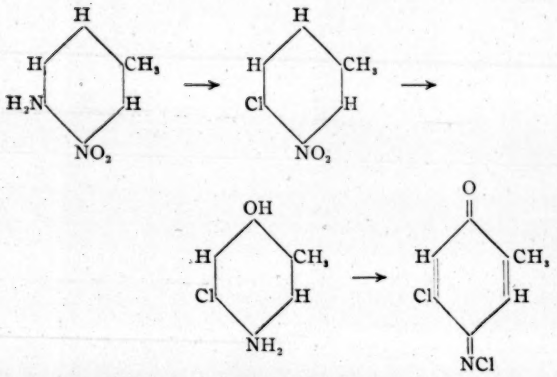
The proof of the structural isomerism of the three chlorimidochlortoluquinones, melting at 91°, 87°, and 65°, respectively, consisted in showing first that not only do the three chlorimides depress each others' melting points, but that all their derivatives—their reduction products, the corresponding aminophenols and their acyl derivatives, the quinones obtained by the oxidation of the aminophenols, and the hydroquinones obtained by the reduction of the quinones—form different series with different melting points and other properties. If the difference were due to space relations of the :NCl group, this difference would vanish with reduction of the group, and identical compounds would result. In the second place, the structure of each of the three chlorimides was brought into definite relations with simpler derivatives of known or readily proved structure.

The chlorimidochlortoluquinone whose melting point is 65° was brought into relation with 3-nitro-4-chlortoluene, and found to have the structure



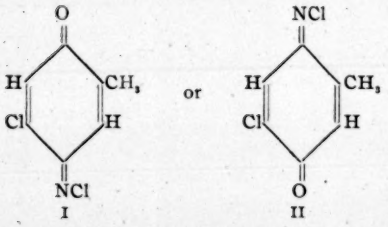
This connection was established by converting *m*-nitro-*p*-toluidine into *m*-nitro-*p*-chlortoluene by the Sandmeyer reaction, transforming this *m*-nitro-*p*-chlortoluene into the corresponding chloraminocresol (melting at 197°–199° with blackening) by electrolytic reduction and rearrangement in concentrated sulphuric acid solution by Gattermann's method,[1] and by converting this chloraminocresol directly into the chlorimide (melting at 65°). The steps may be summarized as follows:

[1] Gattermann and Kaiser: Ber. d. chem. Ges., 18, 2599 (1895).

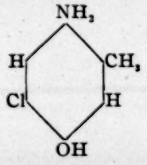


The chlorimidochlortoluquinone that melts at 91° was obtained by the action of hypochlorous acid on the reduction product of Kehrmann's oximes; the oximes in turn were obtained by Kehrmann from so-called *p*-chlortoluquinone in which the chlorine is assumed to be in the para[1] position to the methyl group. The direct proof that such is the case was brought by the oxidation of 4-chlor-3-amino-6-hydroxytoluene, prepared as just described. The same chlortoluquinone (melting at 105°) as that used by Kehrmann in the preparation of his oximes was obtained. The para position of the chlorine atom being thus established, the chlorimide melting at 91° must have the structure

[1] That position for chlorine was generally assumed in the chlortoluquinone from which Kehrmann started, but we can find no direct proof for the assumption. The chlortoluquinone is obtained by oxidation of chlortoluhydroquinone which, in turn, is obtained by the action of hydrochloric acid on toluquinone, in accordance with Schniter's (Ber. d. chem. Ges., **20**, 2286 (1887)) reaction. By the corresponding action of hydrobromic acid on toluquinone, Kehrmann and Rust (Ann. Chem. (Liebig), **303**, 24 (1898)), obtained a bromtoluquinone melting at 105°, and evidently identical with the compound (melting at 106°) in which Gattermann (Ber. d. chem. Ges., **27**, 1931 (1894)) proved definitely that bromine goes into a position para to methyl. But Schniter (Ber. d. chem. Ges., **20**, 1317 (1887)) has shown by his work on thymoquinones that the position taken by chlorine in his reaction is sometimes *not* the same as that taken by bromine.

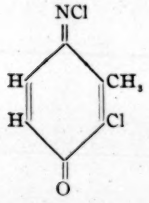


But structure (I) has just been proved to be that of the chlorimide melting at 65°, obtained from the chloraminocresol melting at 197°–199°, which cannot possibly be stereoisomeric, but must be structurally isomeric, with the chloraminocresol that melts at 206°–207°, and which was obtained by the reduction of the chlorimide melting at 91°. The latter, therefore, cannot be stereoisomeric, but must be structurally isomeric, with the chlorimide melting at 65°, and must have structure (II), and its chloraminocresol (melting at 206°–207°) must be 4-chlor-6-amino-3-hydroxytoluene,

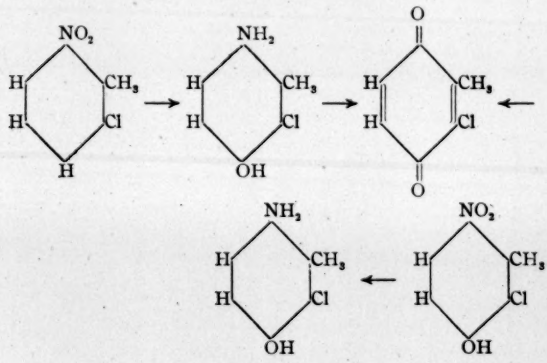


This, it may be added, brings proof, also, of the correctness of the structure assigned by Kehrmann to his stereoisomeric oximes and their derivatives. His own proof, in the light of the above, does not appear unassailable.

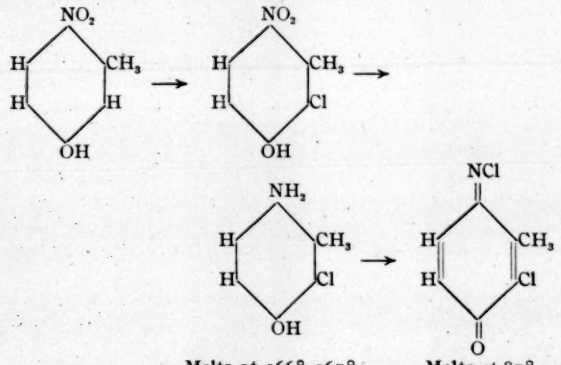
The third chlorimidochlortoluquinone (melting at 87°), first obtained from the chlorination product of *p*-nitro-*m*-cresol, has the structure



The chlortoluquinone obtained by oxidation of its reduction product, chloraminocresol (melting at 166°–167°), was brought by me into relationship with *o*-chlor-*o*-nitrotoluene. This was converted into the corresponding aminocresol by electrolytic reduction in sulphuric acid solution, and from this was obtained, by oxidation, the same chlortoluquinone (melting at 55°) as from the chloraminocresol melting at 166°–167°. The changes are indicated as follows:



In this way the position of the chlorine atom in the chlorimide and its derivatives is established. The position of the chlorimide group is determined by the preparation of the chlorimide from *p*-nitro-*m*-cresol:



Melts at 166°–167° Melts at 87°

The experimental data on which these conclusions are based will now be given:

2-Chlor-4-benzoylamino-5-methylphenyl Benzoate.—This compound was prepared as a further simple derivative to identify Kehrmann's aminocresol, melting at 206°–207°. A portion of the amine was dissolved in a solution of sodium hydroxide, and this was shaken with benzoyl chloride (3 mol.) until the odor of the chloride had about disappeared. The solid that separated was filtered off and repeatedly crystallized from alcohol until it was nearly colorless. It melts at 220°. The substance was found to be soluble in chloroform and ether, but insoluble in a solution of sodium hydroxide. This fact and the figures given on analysis indicate a dibenzoylated compound:

I. 0.5562 gram substance gave 0.0195 gram N (Kjeldahl).
II. 0.3400 gram substance gave 0.0124 gram N.

	Calculated for $C_{21}H_{16}O_3NCl$	Found I	Found II
N	3.83	3.50	3.63

6 - Chlorimido - 4 - chlortoluquinone, $O^{3} : C_6H_2Cl^{4}(CH_3)^{1} : NCl^{6}$.—Five grams of the hydrochloride of the aminocresol obtained

by reduction of Kehrmann's oximes was dissolved in 100 cc. water to which a trace of hydrochloric acid had been added, and the solution cooled to about 0° and then dropped slowly into a cold acidified solution of sodium hypochlorite. The yellow solid that formed was filtered off, washed with cold water and dried. The crude product melted at 88°, and attempts to fractionate it gave lots of crystals having the same melting point, 91°. It is readily soluble in alcohol, chloroform and ligroin, from which latter it is best crystallized, separating in the form of needles radiating from a common center. A warm alcoholic solution of the compound was easily reduced by stannous chloride dissolved in concentrated hydrochloric acid, with the formation of the corresponding chloraminocresol.

The chlorimide was analyzed for chlorine and for nitrogen and gave the following results:

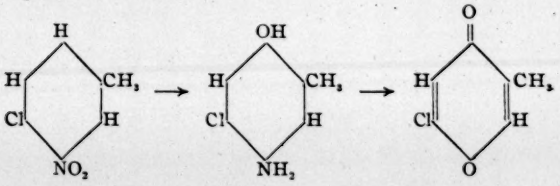
I. 0.2067 gram substance gave 0.3120 gram AgCl.
0.4753 gram substance gave 0.0336 gram N (Kjeldahl).
II. 0.2107 gram substance gave 0.3192 gram AgCl.
0.5351 gram substance gave 0.0376 gram N.

	Calculated for $C_7H_5ONCl_2$	Found I	Found II
Cl	37.32	37.32	37.45
N	7.37	7.06	7.03

Proof of the Structure of p-*Chlortoluquinone.*—For the proof of the structure of the chlortoluquinone which Kehrmann employed in the preparation of his stereoisomeric oximes, and, at the same time, the determination of the position of chlorine in the chlorimide that has just been described, a quantity of pure 3-nitro-4-chlortoluene[1] was first prepared by the Sandmeyer reaction from 3-nitro-4-toluidine, and then reduced electrolytically to an aminocresol by Gattermann's method. For the latter purpose 10 grams of the pure oil was dissolved in 100 grams of sulphuric acid (1.84), and to this solution 0.5 cc. water was added. The liquid so obtained was poured into a porous cup, and the latter placed in a beaker of convenient size so that the distance between the outer

[1] Gattermann and Kaiser: Ber. d. Chem. Ges., **18**, 2599 (1885).

wall of the porous cup and the inner wall of the beaker was about 1.5 cm. Outside the porous cup was placed a mixture of 100 grams of sulphuric acid (1.84) and 5 grams of water. The cathode was placed in the liquid in the porous cup and a current of 7.5 volts and 1.9 to 2.1 amperes was passed for 15 hours. The liquid was then allowed to cool and was poured into six volumes of water. Slight precipitation[1] took place at once, and the mixture stood until it had reached the room temperature and the supernatant liquid was clear. This was next filtered off, and the filtrate, which was deep blue in color, was neutralized with a solution of sodium carbonate. The chloraminocresol formed was precipitated. After filtration the residue was washed with water, and, without further purification, was at once dissolved in very dilute hydrochloric acid, cooled and mixed with a solution of ferric chloride. When the mixture so obtained was distilled with steam, a quinone melting at 105°, and identical with that obtained by oxidizing Kehrmann's chloraminocresol (melting at 206°–207°), passed over. A mixture of the two substances melts at the same temperature as either of them separately. A yield of 60 per cent. was obtained. The reactions may be expressed as follows:



3-Chlorimido-4-chlortoluquinone (melting at 65°), $O:C_6H_2Cl(CH_3):NCl$.—A second portion of the chloraminocresol, obtained from 3-nitro-4-chlortoluene by electrolytic

[1] This precipitate is probably a sulphonic acid. Gattermann found that with *o*-nitrotoluene the chief product was a sulphonic acid of the corresponding aminocresol. Noyes and Clement (Ber. d. chem. Ges., **26**, 991 (1893)) found that the sulphonic acid was not formed when they used sulphuric acid below a certain concentration. In my work some sulphonic acid appeared to form in every case, the amount being smaller when halogen was in the ring.

reduction, was dissolved in dilute hydrochloric acid and the solution cooled to about 0° and then dropped slowly into a cold acidified solution of sodium hypochlorite in the usual way. A chlorimidoquinone, having the characteristic odor, and mixed with some resinous products, was precipitated. It was collected on a filter, washed with cold water and dried. Attempts to fractionate gave portions of solid all having the same melting point, 65°. The compound is soluble in alcohol, ether, and chloroform, but is best crystallized from ligroin, from which it separates in brownish wartlike nodules. Analysis for chlorine indicates that it has the same composition as, and is isomeric with, 6-chlorimido-4-chlortoluquinone, melting at 91°, described above.

0.1965 gram substance gave 0.2969 gram AgCl.

	Calculated for $C_7H_5ONCl_2$	Found
Cl	37.32	37.35

6-Chlorimido-2-chlortoluquinone (melting at 87°), $^{3}O : C_6H_2Cl(CH_3) : {}^{6}NCl$.—The starting point in the preparation of this compound was *m*-cresol, which was obtained by fractionating Kahlbaum's pure product. Fifty grams of the liquid boiling at 199°–200° (uncorr.) was nitrated in accordance with the method of Staedel and Kolb,[1] and the isomeric nitro products that resulted were separated by distillation with steam. The para compound, which is not volatile under these conditioms, and which was obtained in crude form from the distillation residue, was further purified by successive crystallization of its sodium salt from water. These crystals were then decomposed by treatment of their aqueous solution with dilute sulphuric acid, and the free nitrocresol subsequently crystallized from hot water, from which it separated in very nearly colorless needles melting at 127°–129°. A yield of 38 to 40 per cent. was obtained.

*2-Chlor-6-nitro-*m*-cresol,* $^{3}HO.C_6H_2{}^{2}Cl(CH_3){}^{1}{}^{6}NO_2$.—Ten grams of purified 6-nitro-*m*-cresol was chlorinated,[2] the operation

[1] Ann. Chem. (Liebig), **259**, 210 (1890).
[2] *Ibid.*, **303**, 23 (1898).

being started at the room temperature, and the reaction mixture was poured with stirring into six volumes of water. A colorless solid precipitated out at once, and was filtered off and dried on a clay plate. The substance is soluble in benzene, ligroin and chloroform, very soluble in alcohol, and but very slightly soluble in water. After being crystallized twice from benzene it melted sharply at 133°, and this was not changed when a portion of the material was crystallized in the form of its sodium salt, this decomposed by acid, and the free cresol again crystallized from benzene. Analyses[1] for chlorine and for nitrogen gave the following results:

0.2302 gram substance gave 0.1784 gram AgCl.

0.1881 gram substance gave 12.25 cc. N at 21° and 752.5 mm. (uncorr.).

	Calculated for $C_7H_6O_2NCl$	Found
Cl	18.90	19.15
N	7.46	7.34

Hydrochloride of 2-Chlor-6-amino-m-*cresol.*—Five grams of 2-chlor-6-nitro-*m*-cresol was dissolved in hot alcohol and reduced with stannous chloride in the manner already described, forming practically colorless crystals that darkened when heated above 225°, but did not melt when heated as high as 250°. The crystals are readily soluble in water acidulated with hydrochloric acid, in alcohol and in a solution of sodium hydroxide with the formation of a brown liquid. A sample dried *in vacuo* for 72 hours over potassium hydroxide gave the following results when analyzed for chlorine:

0.2674 gram substance gave 0.3966 gram AgCl.

	Calculated for $C_7H_9ONCl_2$	Found
Cl	36.54	36.66

2-Chlor-6-amino-m-*cresol*, $HO.C_6H_2Cl(CH_3)NH_2$ (3, 2, 1, 6).—The free base was easily obtained by treatment of an aqueous solution of the hydrochloride with ammonium carbonate. The precipitate was collected on a filter at once, washed with water

[1] Kehrmann (*loc. cit.*) reports no analyses for the intermediate products through which he obtained proof of the structure of his oximes.

and dried. In this condition the compound was nearly pure, as was shown by the fact that crystallization did not change the melting point. It dissolves in alcohol, benzene, chloroform and solutions of sodium hydroxide, but much less readily in ligroin. Portions were obtained in practically colorless crystals by crystallizing from 75 per cent. alcohol. These melted at 166°–167°, with slight darkening. That this substance could not be an impure specimen of the compound obtained by reducing Kehrmann's oximes was shown by the fact that a mixture of the two melts lower than either of them separately, viz., 157°, as well as by the fact that the derivatives now to be described are not identical with the corresponding compounds obtained from the amine secured by the reduction of the oximes. Analysis for chlorine gave the following results:

0.2982 gram substance gave 0.2716 gram AgCl.

	Calculated for C_7H_8ONCl	Found
Cl	22.50	22.51

4-Acetylamino-5-methyl-6-chlorphenyl Acetate.—In order to further identify this aminocresol, it was converted into an acetyl derivative by warming it with anhydrous sodium acetate and acetic anhydride (1.5 mol.). After recrystallization from benzene, long, colorless, silky needles melting at 178° were secured. A mixture of this substance with the diacetyl derivative (melting at 162°) obtained from 4-chlor-6-amino-*m*-cresol melts at 140°–149°. The new compound did not dissolve in solutions of sodium hydroxide, and this behavior, taken in connection with the percentage of chlorine found upon analysis, indicated a diacetyl derivative:

0.2711 gram substance gave 0.1618 gram AgCl.

	Calculated for $C_{11}H_{12}O_3NCl$	Found
Cl	14.67	14.75

2-Chlortoluquinone, $\overset{3}{O} : C_6H_2\overset{2}{Cl}\overset{1}{CH_3} : \overset{6}{O}$.——The new chloraminocresol was further characterized by conversion of a portion of it into its quinone by treatment with a cold dichromate

mixture. After standing, the precipitate that formed was collected on a filter and dried. A yield of 60 per cent. was obtained. A more convenient method is to mix the cold, slightly acid solution of the hydrochloride of the amine with a solution of ferric chloride, and then to distil the quinone with steam. The quinone is appreciably soluble in water, and is very readily soluble in alcohol, chloroform and ligroin. Crystals deposited from a solution in the latter solvent melted at 55°, and a mixture of the substance with 4-chlortoluquinone, employed by Kehrmann in the preparation of his stereoisomeric oximes, melts at 46°, which shows that the compound in question is a new one. It completes the list of possible chlortoluquinones, the other two being already known, viz., *p*-chlortoluquinone, melting at 105°, prepared by Schniter[1], and *m*-chlortoluquinone, melting at 90°, prepared by Claus and Schweitzer.[2] The syntheses (see below) and anaylsis for chlorine indicate that this compound is isomeric with the substance Kehrmann used as a starting point:

0.2830 gram substance gave 0.2611 gram AgCl.

	Calculated for $C_7H_5O_2Cl$	Found
Cl	22.65	22.79

2-Chlortoluhydroquinone, $HO\overset{3}{C_6}H_2\overset{2}{Cl}(\overset{1}{CH_3})\overset{6}{OH}$.—A portion of 2-chlortoluquinone was mixed with water and the mixture saturated with sulphur dioxide. The yellow color of the quinone was discharged, and after standing overnight in a cool place the solid was nearly colorless. This was filtered off and repeatedly recrystallized from hot water, the filtered solution in each case being decolorized by sulphur dioxide. Short, colorless leaflets melting at 173°, that colored slightly when exposed to the air, crystallized out. These were found to be soluble in alcohol but much less so in chloroform, ligroin, and benzene. In solutions of sodium hydroxide they dissolve, giving first a green color that rapidly changes to a dark red. A mixture of this compound with 4-chlortoluhydro-

[1] Ber. d. chem. Ges., **30**, 2286 (1887).
[2] J. prakt. Chem., [2] **38**, 328 (1888).

quinone, melting at 176°, melts at 146°–158°, which shows that they are not identical. Analysis for chlorine indicates that they are isomeric.

0.3205 gram substance gave 0.2895 gram AgCl.

	Calculated for $C_7H_7O_4Cl$	Found
Cl	22.36	22.33

6-Chlorimido-2-chlortoluquinone, $\overset{3}{O} : C_6H_2\overset{2}{Cl}(\overset{1}{CH_3}) : \overset{6}{N}Cl$. — A portion of the new chloramino-*m*-cresol, melting at 166°–167°, was dissolved in very dilute solution of hydrochloric acid, and this liquid was cooled to about 0° and then dropped slowly into a cold acidified solution of sodium hypochlorite in the usual way. A yellow solid, having the odor characteristic of a chlorimidoquinone, separated out at once. This was filtered off, washed with cold water, and dried on a clay plate. It melted at 86°–87°. All lots of crystals obtained in attempts to fractionate it had the same melting point, 87°. A mixture of this compound with 6-chlorimido-4-chlortoluquinone, melting at 91° (obtained from the chloraminocresol that resulted from the reduction of Kehrmann's oximes), melts at 60°–65°. Analyses for chlorine and for nitrogen gave the following results:

I. 0.1671 gram substance gave 0.2536 gram AgCl.
0.2050 gram substance gave 0.0146 gram N (Kjeldahl).
II. 0.1648 gram substance gave 0.2496 gram AgCl.
0.4864 gram substance gave 0.0353 gram N.

	Calculated for $C_7H_5ONCl_2$	Found I	Found II
Cl	37.32	37.52	37.44
N	7.37	7.12	7.27

Synthesis of 2-Chlortoluquinone

Action of Chlorine on 2-Nitrotoluene.—Janson[1] passed chlorine (1 molecule) into dry 2-nitrotoluene and reports the formation of a chlor compound melting at 37° and boiling at 236°–238°, to which he assigned the structure of 2-nitro-6-chlortoluene. As necessary precautions Janson states that the nitro-

[1] Centralbl., 1900, I, 1110.

toluene must be pure and dry, that a chlorine carrier should be used, and that excess of chlorine must be avoided.

In accordance with these directions, 100 grams of pure dry 2-nitrotoluene, boiling at 218°, obtained by fractionating Kahlbaum's product, was mixed with 2 grams of iron filings dried at 115°, placed in a suitable vessel, and protected from moisture by a tube containing calcium chloride. Into this liquid the calculated amount of chlorine (obtained by the interaction of potassium permanganate and hydrochloric acid) was passed. The operation was begun with the liquid at the room temperature, but 30°–40° was reached during the course of the reaction. When the liquid had cooled it was filtered from the excess of iron, made alkaline with a solution of sodium hydroxide and distilled with steam. The oil that came over was separated from water, dried over calcium chloride and cooled with ice and salt. No crystals[1] were obtained. The oil was next slowly fractionated, a Glinsky distilling tube being used, and the fraction boiling at 236°–238° removed and cooled. Only a very small amount of solid separated.

When the above operation was carried out it was expected that chlorine might enter both ortho and para positions as respects methyl, and thus give rise to the isomers 2-nitro-6-chlortoluene and 2-nitro-4-chlortoluene. In order to prove that this had occurred, 30 grams of the oil (boiling at 236°–238°) was reduced to the corresponding toluidine by means of tin and hydrochloric acid, after which the mixture was made alkaline and distilled with steam. The oil that came over was dried and fractionated and the portion obtained between 237°–245°[2] was next boiled for ten hours with glacial acetic acid and the mixture poured into 500 cc. water. The acettoluide that separated was filtered off and fractionally crystallized as follows:

The entire mass was dissolved in boiling water and the liquid filtered through paper and allowed to come to the

[1] Janson states that at this point he was able to obtain crystals.

[2] 4-Chlor-2-toluidine boils at 237° (Goldschmidt and Honig: Ber. d. chem. Ges., 19, 2440 (1886)), and 6-chlor-2-toluidine boils at 245° (Wynne and Greeves: Centralbl., 1898, II, 530).

room temperature. The crystals that had formed were removed and further fractionated by treatment of their warm chloroform solution with one volume of ligroin (60°–80°). Three crystallizations in this manner gave a fraction that melted sharply at 154°.[1] The aqueous filtrate that had been set aside meanwhile was now placed in the refrigerator and allowed to stand overnight. The solid that formed was removed and crystallized from hot water, and gave colorless needles that melted at 130°–131°.[2] When these were dissolved in hot chloroform and the solution was mixed with enough ligroin (60°–80°) to cause slight precipitation, warmed until solution occurred and then set aside to cool, the crystals that formed melted at 136°–137°.

In order to determine whether this low-melting acettoluide is identical with Goldschmidt and Honig's[3] product, some of the latter was prepared according to the directions given by these chemists, the start being made with pure 4-chlortoluene. When the acettoluide was crystallized once from water, it melted at 130°–131°, as stated in the literature, but further crystallization from chloroform and ligroin, as specified above, raised the melting point to 136°–137°, and a mixture of this product with the low-melting compound obtained from Janson's oil melted at the same temperature as either of them separately, which proves that they are identical. A mixture of either of these with the high-melting acettoluide, melting at 154°, softens at 110°, and is entirely melted at 123°. From this it follows that chlorination of 2-nitrotoluene gives both 4-chlor-2-nitrotoluene and 6-chlor-2-nitrotoluene.

Electrolytic Reduction of the Mixture of Chlornitrotoluenes.—Ten grams of the oil boiling at 236°–238°, obtained by chlorinating *o*-nitrotoluene, was dissolved in 100 grams of sulphuric acid (1.84), and this solution diluted with 2 cc. water. Through this a current of 7.5 volts and 2.2 amperes was passed for ten hours, at the end of which time the liquid was poured into 360 cc. water and the mixture set aside to

[1] Wynne and Greeves (*loc. cit.*) and Janson (*loc. cit.*) found the melting point of the acettoluide from *o*-chlor-*o*-toluidine to be 157°–159°.

[2] Goldschmidt and Honig: *Loc. cit.*

[3] *Ibid.*

cool. It was next filtered, and the filtrate, which was deep purple in color, was cooled to about 0°, and 25 grams of powdered sodium dichromate was slowly added to oxidize the aminophenols produced to their corresponding quinones. The resulting mixture was allowed to come to room temperature during an hour, and was then distilled with steam. The yellow solid that passed over was dried and found to melt at 48°–51°, which suggested a mixture of the *p*- and *o*-chlortoluquinones, corresponding to the positions of chlorine already indicated by the acettoluides described.

A portion of this mixture was fractionated by crystallization from ligroin (40°–60°), and there was obtained a fraction that separated in the form of yellow prisms melting at 105°, and was found to be identical with 4-chlortoluquinone, a mixture of the two still melting at 105°. When mixed with 2-chlortoluquinone, melting at 55°, the melting point was depressed exactly as stated on page 450. The combined mother liquors were allowed to evaporate, but the crystals obtained from them did not melt sharply, and repeated crystallization did not change this.

A second portion of the dried crude quinone, melting at 48°–51°, mentioned above, was fractionally sublimed[1] at a temperature of 45°–50° and a pressure of 15–17 mm. The process was very slow, and complete separation was not secured. The sublimate melted at 48°–51° and behaved like 2-chlortoluquinone containing a trace of the isomeric 4-chlortoluquinone. The sublimate was next mixed with a little water, and saturation of this with sulphur dioxide gave a hydroquinone which, after one subsequent crystallization from water, melted at 173° and did not depress the melting point of 2-chlortoluhydroquinone, melting at 173°, described on page 450. A mixture of this new product with 4-chlortoluhydroquinone, melting at 176°, melts at 147°–151°, showing that the new product is not identical with 4-chlortoluhydroquinone.

A third portion of the dried crude quinone was reduced to hydroquinone, and gave crystals melting at 148°–152°, indi-

[1] Kempf: J. prakt. Chem., [2] **78**, 203 (1909).

cating the presence of a mixture. This was dissolved in hot benzene,[1] the liquid filtered through cotton, the filtrate allowed to cool to the room temperature, and the crystals immediately removed. Recrystallization in this way three times and final crystallization from water gave a product melting at 174°–175°. A mixture of this with 2-chlortoluhydroquinone, melting at 173°, melted at 173°–175°, while with 4-chlortoluhydroquinone the melting point was depressed to 147°–151°.

It is thus clear that the mixture of 2-chlor-6-nitrotoluene and 4-chlor-6-nitrotoluene obtained by chlorinating *o*-nitrotoluene, whose structures were proved on the preceding pages, gives by electrolytic reduction and rearrangement in sulphuric acid solution the corresponding pair of aminophenols, viz., 1-methyl-2-chlor-6-aminophenol and 1-methyl-4-chlor-6-aminophenol, which in turn give by oxidation the two chlortoluquinones, viz., *p*-chlortoluquinone, melting at 105°, and *o*-chlortoluquinone, melting at 55°. The latter is identical with the chlortoluquinone, melting at 55°, obtained by oxidizing the chloraminocresol, melting at 166°–167°, produced by the action of chlorine on *p*-nitro-*m*-cresol, and subsequent reduction. It is thus shown that the chlorine atom enters into the ortho position to the methyl group in *p*-nitro-*m*-cresol and that it has that position in all the derivatives obtained from the chlorinated nitro-*m*-cresol, viz., the chloraminocresol, melting at 166°–167°,[2] and the chlorimidochlortoluquinone, melting at 87°.

SUMMARY

The most important results of the work described in this paper may be summarized as follows:

1. (*a*) When *p*-nitro-*m*-cresol is chlorinated by passing chlorine, diluted with carbon dioxide, into a glacial acetic

[1] It had previously been noted that these two compounds differed in the rapidity with which crystals were deposited from benzene solution, 2-chlortoluhydroquinone separating more quickly than its isomer.

[2] The work will be continued, and attempts made to isolate directly the chloraminocresols produced by the electrolytic reduction in sulphuric acid solution as described on page 445.

acid solution of the nitro compound, chlorine takes a position adjacent to methyl.[1]

(*b*) *o*-Chlortoluquinone, the last of the three possible chlortoluquinones, was prepared by oxidation of the aminocresol obtained by reducing the chlorinated nitrocresol.

2. When *o*-nitrotoluene is chlorinated in the presence of iron, a mixture of the *o*- and the *p*-chlor-*o*-nitrotoluenes results.

3. When 2,4,6-tribrom-*m*-cresol is nitrated under certain conditions it gives rise to two isomeric mononitro derivatives, viz., 2,6-dibrom-4-nitro-*m*-cresol and 2,4-dibrom-6-nitro-*m*-cresol, while 2,4,6-trichlor-*m*-cresol could not be nitrated under any conditions employed in this work.

4. The chlorimidoquinones obtained as end products in these experiments do not appear to exist in stereoisomeric forms. Chlorimidochlortoluquinone was obtained in three forms, melting at 91°, 87°, and 65°, respectively, but they were proved to be structural isomers and not stereoisomers.

In conclusion, I hereby tender my sincere thanks to Professor Stieglitz for the painstaking scrutiny with which he has guided this work.

[Contributions from the Sheffield Laboratory of Yale University]

CXCIV.—ON HYDANTOINS

THE ACTION OF ACYLTHIONCARBAMATES, ACYLDITHIOCARBAMATES AND ACYLIMIDODITHIOCARBONATES ON α-AMINO ACIDS

2-THIOHYDANTOIN

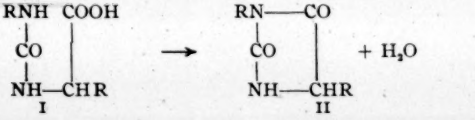
By Henry L. Wheeler, Ben H. Nicolet and Treat B. Johnson

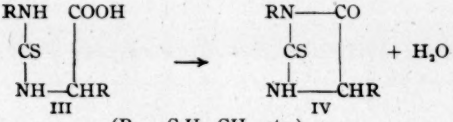
[SIXTH PAPER]

It is known that the alkyl isocyanates and alkyl isothiocyanates (mustard oils) combine with α-amino acids, forming hydantoic acids, (I) and (III), which then undergo inner con-

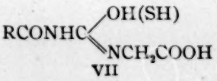
[1] Taking Kehrmann's results, as well as my own, into consideration, one would be inclined to conclude that mixtures of this compound and its isomer, with the chlorine atom in a position para to the methyl group, are formed. In this work the formation of the ortho derivatives is conclusively proved.

densations, giving the corresponding 1-alkylhydantoins[1] (II) and 1-alkylthiohydantoins[2] (IV), respectively. The action of acyl isocyanates, RCONCO, and the corresponding acyl isothiocyanates, RCONCS, on amino acids has not been investigated. The specific aim of the work described in this paper was to synthesize some N-acyl derivatives of hydantoic and thiohydantoic acids, (V) and (VI), and investigate their behavior on hydrolysis and also the reactivity of their methylene hydrogens, $=N—CH_2—CO$, towards aldehydes. We shall describe also some interesting derivatives of the *pseudo* forms of these acids (VII). Hydantoic acid derivatives of these types have not hitherto been described.





(R = C_6H_5, CH_3, etc.)



The action of amines on the four classes of acylcarbamates, (X), (XII), (XIV), and (XV), has been investigated in this laboratory. Ethyl acetylcarbamate (acetylurethane), which

[1] Kuhn: Ber. d. chem. Ges., **27**, 2880. Paal: *Ibid.*, **27**, 975 (1894). Mouneyrat: *Ibid.*, **33**, 2393. Fischer: *Ibid.*, **33**, 2370 (1900). Fischer and Mouneyrat: *Ibid.*, **33**, 2383. Neuberg and Manasse: *Ibid.*, **38**, 2359. Neuberg and Rosenberg: Biochem. Z., **8**, 459.

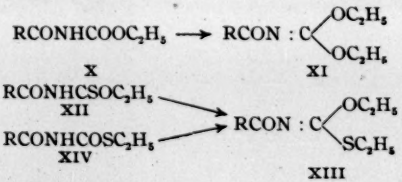
[2] Aschan: Ber. d. chem. Ges., **17**, 420 (1884). Marckwald, Neumark and Stelzner: *Ibid.*, **24**, 3278 (1891). Wheeler and Brautlecht: THIS JOURNAL, **45**, 446 (1911). Brautlecht: J. Biol. Chem., **10**, 139.

was thoroughly investigated by Young and Clark,[1] reacts with bases, giving as chief products normal ureas. Ethyl benzoylcarbamate (VIII) reacts in a similar manner with aniline, for example, giving benzoylphenylurea (IX) and alcohol.[2] Acylthiolcarbamates (XIV) and acyldithiocarb-

$$\underset{\text{VIII}}{C_6H_5CONHCOOC_2H_5} + C_6H_5NH_2 = \underset{\text{IX}}{C_6H_5CONHCONHC_6H_5} + C_2H_5OH$$

amates (XV) react with bases in a manner analogous to that of the oxygen derivatives, forming acylureas and acylthioureas, respectively, with evolution of mercaptans.[3] The acylthioncarbamates (XII), on the other hand, react in an abnormal manner with bases, forming addition products which break down with evolution of hydrogen sulphide, giving acylpseudoureas.[4]

Of the three classes of acylimidocarbonates, (XI), (XIII) and (XVI), only the acylimidothio- and acylimidodithiocarbonates, (XIII) and (XVI), have been studied. They both react smoothly with amines. The monothiocarbonates give the same acylpseudoureas as are obtained by the action of bases on the acylthioncarbamates[5] (XII). The acylimidodithiocarbonates react with bases, with evolution of mercaptans, forming acylpseudothioureas.[6] Acylimidocarbonates, represented by formula (XI), have not been synthesized.[7]



[1] J. Chem. Soc., **73**, 361 (1898).
[2] Wheeler and Merriam: J. Am. Chem. Soc., **23**, 289 (1901).
[3] Wheeler and Merriam: *Loc. cit.*
[4] Wheeler and Johnson: THIS JOURNAL, **24**, 190 (1900); **27**, 218 (1902).
[5] Wheeler and Johnson: *Loc. cit.*
[6] Wheeler and Johnson: THIS JOURNAL, **26**, 408.
[7] The writer desires to call attention to the fact that Mr. Lewis H. Chernoff is now working on a method of synthesizing these compounds. The results will be published later.—T. B. JOHNSON.

$$\underset{\text{XV}}{RCONHCSSC_2H_5} \longrightarrow \underset{\text{XVI}}{RCON : C\begin{matrix}SC_2H_5\\SC_2H_5\end{matrix}}$$

(R = C_6H_5, CH_3, etc.)

Table I

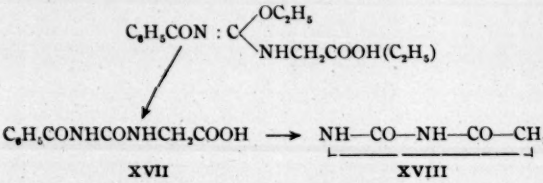
$$RCONHCSOR' + NH_2CH_2COOH = RCON : C\begin{matrix}OR'\\NHCH_2COOH\end{matrix} + H_2S$$

Acylthiocarbamates	Amino acid or ester	Acylpseudohydantoic acid derivative	Melting point
$C_6H_5CONHCSOC_2H_5$[1]	$NH_2CH_2COOC_2H_5$	$C_6H_5CON : C\begin{matrix}OC_2H_5\\NHCH_2COOC_2H_5\end{matrix}$	79°–80°
$C_6H_5CONHCSOC_2H_5$	NH_2CH_2COOH	$C_6H_5CON : C\begin{matrix}OC_2H_5\\NHCH_2COOH\end{matrix}$	161°
$C_6H_5CONHCSOCH_3$[1]	$NH_2CH_2COOC_2H_5$	$C_6H_5CON : C\begin{matrix}OCH_3\\NHCH_2COOC_2H_5\end{matrix}$	103°

[1] Lössner: *J. prakt. Chem.* [2] **10**, 237 (1874). Miquel: *Ann. chim. phys.* [5] **11**, 318 (1877). Dixon: *J. Chem. Soc.*, **1899**, 380. Wheeler and Johnson: *Loc. cit.*

The action of amino acids or their esters on acylcarbamates and acylimidocarbonates (sulphur and oxygen compounds) has not been investigated. We have now examined the behavior of glycocoll and its ethyl ester towards acylthioncarbamates (XII), acyldithiocarbamates (XV) and acylimidodithiocarbonates (XVI). The acylthioncarbamates reacted smoothly with this amino acid, in the presence of alkali, and with its ester in the same manner as with amines, forming alkyl derivatives of acylpseudohydantoic acids. The thioncarbamates which were used in our work and the pseudohydantoic acid derivatives prepared from them are tabulated above for inspection.

Benzoylpseudoethylhydantoic acid and its ethyl ester were converted into the normal benzoylhydantoic acid (XVII) when heated with dilute hydrochloric acid. If, however, concentrated hydrochloric acid was used this benzoylhydantoic acid also underwent hydrolysis, forming benzoic acid and hydantoin (XVIII).



The acylthiohydantoic acids (VI) and their esters theoretically should be formed by the action of acyl isothiocyanates on amino acids and their esters, respectively:

$$RCONCS + NH_2CH_2COOH = RCONHCSNHCH_2COOH$$

We did not, however, employ these rhodanides for the preparation of this new class of compounds. We found that they were formed smoothly by the action of the potassium salts and esters of amino acids, respectively, on the acyldithiocarbamates. The representatives of this new class of compounds, which were prepared by the action of glycocoll and alanine on dithiocarbamates, are represented in the following table:

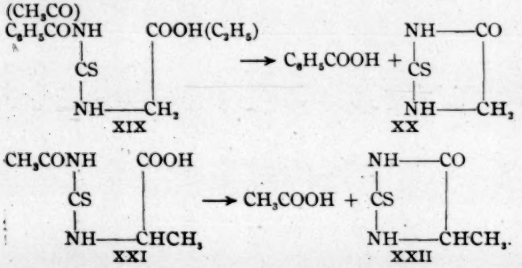
Table II

$$RCONHCSSR' + NH_2CH_2COOH = RCONHCSNHCH_2COOH + R'SH$$

Acyldithiocarbamates	Amino acid or ester	Acylthiohydantoic acid or ester	Melting point
$C_6H_5CONHCSSC_2H_5$	$NH_2CH_2COOC_2H_5$	$C_6H_5CONHCSNHCH_2COOC_2H_5$	128°–129°
$C_6H_5CONHCSSC_2H_5$	NH_2CH_2COOH	$C_6H_5CONHCSNHCH_2COOH$	202°
$CH_3CONHCSSC_2H_5$	$NH_2CH_2COOC_2H_5$	$CH_3CONHCSNHCH_2COOC_2H_5$	104°–105°
$CH_3CONHCSSC_2H_5$	NH_2CH_2COOH	$CH_3CONHCSNHCH_2COOH$	225°–227°
$CH_3CONHCSSC_2H_5$	$NH_2CH(CH_3)COOH$	$CH_3CONHCSNHCH(CH_3)COOH$	171°

When these acylthiohydantoic acids or their esters (VI) were digested with hydrochloric acid they behaved like the corresponding oxygen acids and were transformed into cyclic compounds. For example, we found that benzoyl- and acetyl-

thiohydantoic acids (XIX) underwent hydrolysis under these conditions, and that the unknown 2-thiohydantoin (XX) was formed in both cases. 1-Acetyl-4-methylthiohydantoic acid (XXI) underwent a similar transformation, giving 2-thio-4-methylhydantoin (XXII):



These nitrogen-unsubstituted thiohydantoins (XX) and (XXII) represent new types of thiohydantoins. Their formation, in this manner, from the acylthiohydantoic acids is remarkable since the plain ethyl thiohydantoate,

$$NH_2CSNHCH_2COOC_2H_5$$

undergoes no condensation under similar conditions, while hydantoic acid and its esters condense quantitatively to hydantoin.[1] Harries and Weiss write as follows regarding the behavior of the thiohydantoic ester:

"Ein Versuch den Thiohydantoinsäureester durch Schmelzen oder Behandeln mit Salzsäure in das neutrale Thiohydantoin umzuwandeln führte zu keinem positiven Erfolge."

These investigators were also unable to introduce a sulphur atom into hydantoin by heating it with phosphorus trisulphide. They also heated hydantoin with ammonium sulphide, a reagent which was used successfully by Fischer[2] for introducing sulphur in the purine series, but it was com-

[1] Harries and Weiss: Ann. Chem. (Liebig), **327**, 355 (1903); Ber. d. chem. Ges., **33**, 3418 (1900). Bailey: THIS JOURNAL, **28**, 386.

[2] Ann. Chem. (Liebig), **288**, 159.

pletely decomposed under these conditions and glycocoll was formed. The fact that the benzoyl- and acetylthiohydantoic esters condense to 2-thiohydantoin when heated with hydrochloric acid, while ethyl thiohydantoate undergoes no condensation under the same conditions, indicates that the acyl derivatives first condense, giving as intermediate products acylthiohydantoins. These, being unstable in the presence of hydrochloric acid, then undergo hydrolysis, giving the plain 2-thiohydantoins.

Diethyl benzoylimidodithiocarbonate[1] reacted normally with aminoacetic acid and its ethyl ester, giving the alkyl derivatives of the pseudo forms of benzoylthiohydantoic acid and ethyl benzoylthiohydantoate, respectively (Table III).

The acylhydantoic and acylthiohydantoic acids, (V) and (VI), may be viewed as acylcarbamyl- and acylthioncarbamyl derivatives of glycocoll corresponding to the benzoyl derivative of this amino acid, or hippuric acid. Since they all contain the grouping —NH.CH_2.CO— it was therefore of especial interest to examine their behavior towards aldehydes. Plöchl[2] was the first to show that hippuric acid condenses with aldehydes, but it was Erlenmeyer[3] who correctly explained the nature of the condensation products.

We have now made the interesting observation that benzoyl- and acetylthiohydantoic acids condense readily with benzaldehyde when boiled in acetic acid solution and in presence of sodium acetate and acetic anhydride, forming benzoyl- and acetylbenzalthiohydantoins, (XXIII) and (XXV), respectively. On the other hand, under the same conditions, we obtained no condensation products with the esters of these two acids. An attempt to condense benzoylhydantoic acid (XVII) with benzaldehyde was also unsuccessful. This latter observation is of interest because it again illustrates the greater tendency of the sulphur compounds to condense, as was observed by Wheeler and Brautlecht[4] in the case of the phenylthiohydantoins.

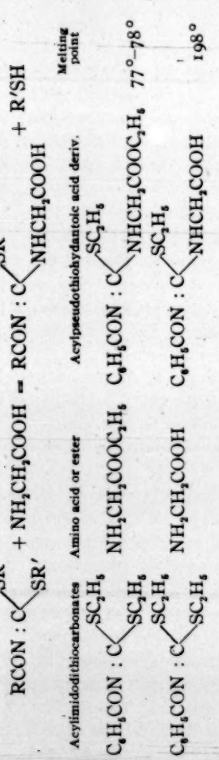
[1] Wheeler and Johnson: *Loc. cit.*

[2] Ber. d. chem. Ges., **16**, 2815 (1883).

[3] Ann. Chem. (Liebig), **271**, 137; **275**, 1. Erlenmeyer and Stadlin: *Ibid.*, **337**, 283, 265. Erlenmeyer and Arbenz: *Ibid.*, **337**, 302.

[4] This Journal, **45**, 446 (1911).

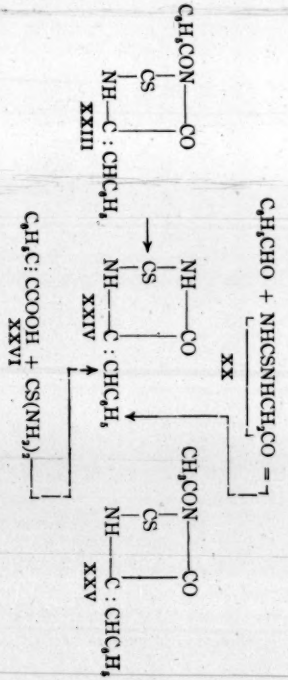
Table III



When benzoylbenzalthiohydantoin (XXIII) was warmed with alkali the benzoyl group was removed and benzalthiohydantoin (XXIV) was formed. This same benzal compound was also obtained by condensation of thiohydantoin (XX) with benzaldehyde. Ruhemann and Stapleton[1] have assigned

[1] J. Chem. Soc., 77, 246.

this same structure to a compound obtained by them by condensation of thiourea with phenylpropiolic acid (XXVI). Our compound agreed apparently with their product in all its properties except the melting point. They give the melting point as 280° on slow heating or 300° on heating rapidly. Our compound, which was made by two methods, melted in both cases at 258° when heated in a capillary tube slowly or rapidly.



EXPERIMENTAL PART

Ethyl Benzoylpseudoethylhydantoate, $C_6H_5CON : C(OC_2H_5)NH.CH_2COOC_2H_5$.—Ethyl aminoacetate and ethyl benzoylthioncarbamate[1] react slowly at ordinary temperature with evolution of hydrogen sulphide. When equivalent quantities of the two esters were heated on the steam bath, a condenser being used to prevent loss of the acetate, the reaction was complete within 15 minutes and a 65–70 per cent. yield of the hydantoate was obtained. The compound crystallizes from 95 per cent. alcohol in slender, colorless, rectangular plates, which melt at 79°–80° to a clear oil and decompose above 200°. The ester is very soluble in boiling alcohol, moderately soluble in cold and soluble in hot water. Analysis (Kjeldahl):

	Calculated for $C_{14}H_{18}O_4N_2$	Found
N	10.05	9.90

Ethyl Benzoylpseudomethylhydantoate, $C_6H_5CON : C(OCH_3)NHCH_2COOC_2H_5$.—From ethyl aminoacetate and methyl benzoylthioncarbamate.[2] It forms colorless, transparent prisms melting at 103°. Analyses (Kjeldahl):

	Calculated for $C_{13}H_{16}O_4N_2$	Found	
		I	II
N	10.60	10.77	10.63

Benzoylpseudoethylhydantoic Acid, $C_6H_5CON : C(OC_2H_5)NHCH_2COOH$.—One and nine-tenths grams of aminoacetic acid were dissolved in 10 cc. of water containing 1.5 grams of potassium hydroxide, and 5.3 grams of ethyl benzoylthioncarbamate, in 10 cc. of alcohol, was added to the solution. There was an immediate reaction with evolution of hydrogen sulphide. After heating 2 hours on the steam bath the solution was then concentrated to 10 cc., cooled and acidified with acetic acid. The hydantoic acid separated and was purified by crystallization from alcohol. It separated in needles which melted at 161° to a turbid oil

[1] Wheeler and Johnson: *Loc. cit.*
[2] Miquel: *Loc. cit.*

which finally became clear at 203°. While this behavior on melting indicated a mixture, the nitrogen determinations (Kjeldahl) agreed with the calculated value for the hydantoic acid:

	Calculated for $C_{12}H_{14}O_4N_2$	Found I	Found II
N	11.20	11.20	11.19

Benzoylhydantoic Acid, $C_6H_5CONHCONHCH_2COOH$.—This acid was prepared by hydrolysis of benzoylpseudoethylhydantoic acid or ethyl benzoylpseudomethylhydantoate with hydrochloric acid. There was some difficulty in choosing conditions most favorable for the change since the benzoyl group is removed by too long hydrolysis. The best yields, about 60 per cent., were obtained by digesting the acid for 4 to 5 hours with equal parts of water and concentrated hydrochloric acid. Ethyl benzoylpseudomethylhydantoate underwent only partial conversion into the hydantoic acid after digestion with hydrochloric acid of the above concentration for 30 minutes. During the digestion a gas was evolved which burned with a green flame and was identified as methyl chloride. The hydantoic acid crystallizes in plates which melt at 253°–254° with effervescence. It is difficultly soluble in hot alcohol, practically insoluble in cold alcohol and water. Analysis (Kjeldahl):

	Calculated for $C_{10}H_{10}O_4N_2$	Found
N	12.15	12.28

Conversion of the Hydantoic Acid into Hydantoin.—Two grams of the benzoylhydantoic acid were suspended in 100 cc. of concentrated hydrochloric acid, 40 cc. of water added and the solution evaporated to dryness on the steam bath. One and two-tenths grams of the acid were recovered unaltered, and in the alcoholic extract of the residue only benzoic acid and hydantoin were identified, No benzoylhydantoin was detected.

Attempt to Condense Benzoylhydantoic Acid with Benzaldehyde.—The hydantoic acid was recovered unaltered after long digestion with benzaldehyde in glacial acetic acid solution in

the presence of acetic anhydride and anhydrous sodium acetate. Analysis (Kjeldahl):

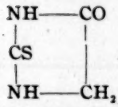
	Calculated for $C_{10}H_{10}O_4N_2$	Found
N	12.15	12.4

Ethyl Benzoylthiohydantoate, $C_6H_5CONHCSNHCH_2COOC_2H_5$.—When ethyl benzoyldithiocarbamate and ethyl aminoacetate were mixed in molecular proportions there was an immediate reaction with evolution of mercaptan. The reaction was complete after heating on the steam bath for about 15 minutes. We obtained a crystalline mass which was dissolved in alcohol, digested for about 4 hours and then cooled, when the ester separated in needles melting at 128°–129° to a pale yellow oil. The compound is very soluble in boiling alcohol, moderately soluble in cold and slightly soluble in hot water. Analysis (Kjeldahl):

	Calculated for $C_{12}H_{14}O_3N_2S$	Found
N	10.51	10.35

Benzoylthiohydantoic Acid, $C_6H_5CONHCSNHCH_2COOH$.—Five grams of aminoacetic acid and 3.8 grams of potassium hydroxide were dissolved in 30 cc. of water, and 15 grams of ethyl benzoyldithiocarbamate (1 mol.) in 30 cc. of alcohol added to the aqueous solution. After 8 hours' digestion on the steam bath the solution was evaporated to dryness and the residue digested with 600 cc. of water. After cooling the solution and acidifying with hydrochloric acid the above hydantoic acid separated in the form of needles. It crystallizes from alcohol in needles and from water in plates which melt at 202°. The acid is very soluble in hot alcohol, moderately soluble in cold and difficultly soluble in hot water. The yield was about 75 per cent. of the calculated. Analysis (Kjeldahl):

	Calculated for $C_{10}H_{10}O_3N_2S$	Found
N	11.75	11.41



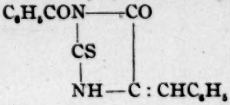
2-Thiohydantoin, .—This thiohydantoin can be prepared either from benzoylthiohydantoic acid or acetylthiohydantoic acid (see below). Benzoylthiohydantoic acid was digested for 10-12 hours with about five times its weight of concentrated hydrochloric acid. The solution wash ten allowed to evaporate to dryness and sufficient alcohol added to dissolve the residue on heating. On cooling, the thiohydantoin separated in yellow prisms which decomposed slowly above 200° and finally melted at 227°. This compound is readily soluble in warm alcohol and water and moderately soluble in cold. Analysis (Kjeldahl):

	Calculated for $C_3H_4ON_2S$	Found I	Found II	Found III
N	24.12	23.68	24.04	24.17

Acetylthiohydantoic acid or its ethyl ester are both converted into this thiohydantoin by digestion with hydrochloric acid. The method finally used for making the thiohydantoin in large quantities was as follows: The ethyl acetylthiohydantoate was prepared as described below and the solution evaporated to dryness. The residue was then digested several hours with concentrated hydrochloric acid and again evaporated to dryness and the thiohydantoin then separated from potassium chloride by extraction with alcohol. The yield was 62 per cent. of the calculated.

Condensation of Benzoylthiohydantoic Acid with Benzaldehyde

1-Benzoyl-4-benzalthiohydantoin,

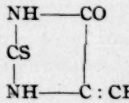


.—Five grams of benzoylthiohydantoic acid and 3 grams of benzaldehyde were dissolved in 25 cc. of glacial acetic acid, and 3.5 grams of fused sodium acetate and 4.3 grams of acetic anhydride added to the solution. The mixture was then heated to boiling, in an oil bath, for

45 minutes. The solution assumed, under these conditions, a blood-red color. On cooling and adding water, 2.2 grams of the benzoylthiohydantoin were precipitated, and after concentrating the filtrate more was obtained. The yield was 3.6 grams, corresponding to 56 per cent. of the calculated. The hydantoin is moderately soluble in boiling alcohol and separates in rectangular plates which melt at 181° to a red oil and then decompose when heated above 260°. Its behavior on melting indicated a ring structure and not that of a hydantoic acid, as these generally melt with effervescence. It is insoluble in water. Analysis (Kjeldahl):

	Calculated for $C_{17}H_{12}O_2N_2S$	Calculated for $C_{17}H_{14}O_3N_2S$	Found
N	9.10	8.59	9.07

An attempt to condense benzaldehyde with ethyl benzoylthiohydantoate, under the same conditions as described in this experiment, was unsuccessful. The ester was recovered unaltered.

4-Benzalthiohydantoin,  .—This compound was formed when the corresponding benzoylhydantoin, described in the preceding experiment, was dissolved in cold 10 per cent. potassium hydroxide solution. On neutralizing the alkaline solution with acetic acid the benzalthiohydantoin separated as an oil which soon crystallized in the form of microscopic, yellow needles. It crystallizes from alcohol in yellow needles melting at 258° with slight decomposition. Analysis (Kjeldahl):

	Calculated for $C_{10}H_8ON_2S$	Found
N	13.70	13.57

Ruhemann and Stapleton[1] state that this compound melts at 280° on slow heating and 300° on heating rapidly. Our product melted at 258° when heated rapidly, and also at this

[1] *Loc. cit.*

same temperature after being held at 240°–250° for three minutes before raising the temperature to that of its melting point. The same benzalthiohydantoin was also obtained by condensation of thiohydantoin with benzaldehyde in glacial acetic acid solution and in the presence of sodium acetate. It melted at 258° and a mixture of this benzal compound with some prepared from the benzoylthiohydantoin melted at exactly the same temperature.

Benzalthiohydantoin is very stable in the presence of alkali. One-half a gram was dissolved in 12 per cent. potassium hydroxide solution and this then heated at 100° for one hour. The solution was then cooled and acidified with hydrochloric acid, when the unaltered hydantoin deposited. It melted at 258°.

Ethyl Benzoylpseudoethylthiohydantoate, $C_6H_5CON : C(SC_2H_5)NHCH_2COOC_2H_5$.—This ester was prepared by the action of ethyl aminoacetate on diethyl benzoylimidodithiocarbonate.[1] They reacted at ordinary temperature with evolution of mercaptan and after standing overnight the mixture completely solidified. The yield was practically quantitative. The ester is very soluble in alcohol and separates from saturated solutions, on cooling, in flakes melting at 77°–78° to a clear oil. Analysis (Kjeldahl):

	Calculated for $C_{14}H_{18}O_3N_2S$	Found
N	9.53	9.26

This ester does not add methyl iodide. Some of the compound was dissolved in an excess of methyl iodide and the solution allowed to stand for 4 days. After evaporation of the iodide the hydantoate was recovered unaltered and melting at 77°. There was no evidence of any reaction.

Benzoylpseudoethylthiohydantoic Acid, $C_6H_5CON : C(SC_2H_5)NHCH_2COOH$.—From aminoacetic acid and diethyl benzoylimidodithiocarbonate. The manipulation was the same as in the condensation of glycocoll with ethyl benzoyldithiocarbamate (above). After heating on the steam bath for 7 hours the mixture was concentrated to

[1] Wheeler and Merriam: *Loc. cit.*

10 cc., washed with ether to remove any unaltered ester and the hydantoic acid then precipitated by addition of acetic acid. The acid was colored violet but on recrystallization from boiling alcohol it separated in clusters of colorless needles which melted at 198°. The yield was about 65 per cent. of the calculated. The acid is readily soluble in boiling alcohol, moderately soluble in cold, and difficultly soluble in water. The acid undergoes slight decomposition on prolonged heating at 100°. Analyses (Kjeldahl):

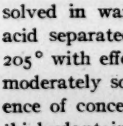
	Calculated for $C_{12}H_{14}O_3N_2S$	Found I	Found II	Found III
N	10.5	9.72	9.98	9.88

Acetylthiohydantoic Acid, $CH_3CONHCSNHCH_2COOH$.—This acid was prepared by the action of aminoacetic acid on ethyl acetyldithiocarbamate. The procedure was the same as in the preparation of benzoylthiohydantoic acid. After heating for 22 hours the solution was concentrated and acidified with acetic acid. On cooling, the potassium salt of the hydantoic acid separated in colorless prisms which melted at 225°–227° with effervescence. Analysis (Kjeldahl):

	Calculated for $C_5H_7O_3N_2SK$	Found
C	13.08	13.52

In order to obtain the free acid the potassium salt was dissolved in warm, dilute hydrochloric acid. On cooling, the acid separated in slender, colorless needles which melted at 205° with effervescence. The acid is very soluble in hot and moderately soluble in cold water. When heated in the presence of concentrated hydrochloric acid it is converted into thiohydantoin.

1-Acetyl-2-thio-4-benzalhydantoin,



.—Acetylthiohydantoic acid was dissolved in 5 times its weight of glacial acetic acid, and 1.2 and 2.0 molecular proportions of benzaldehyde and sodium ace-

tate, respectively, added to the solution. After heating one hour a portion of the mixture was diluted with water. No precipitate resulted. Two molecular proportions of acetic anhydride were then added and the solution digested for another hour. It had assumed a deep red color and on adding water the benzalhydantoin immediately separated. The presence of acetic anhydride is apparently necessary, in this case, to effect a condensation. This acetylhydantoin is readily soluble in boiling alcohol and insoluble in water. It crystallizes from alcohol in light yellow prisms which melt at 231° to a clear red oil. Analysis (Kjeldahl):

	Calculated for $C_{12}H_{10}O_2N_2S$	Found
N	11.37	11.42

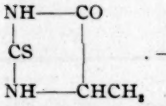
An attempt to condense ethyl acetylthiohydantoate (see below) with benzaldehyde under the above conditions was unsuccessful.

Ethyl Acetylthiohydantoate, $CH_3CONHCSNHCH_2COOC_2H_5$.—This was prepared by warming, in alcoholic solution, ethyl aminoacetate with ethyl acetyldithiocarbamate. It crystallizes in hexagonal prisms which melt at 104°–105° to a clear colorless oil. Analysis (Kjeldahl):

	Calculated for $C_7H_{12}O_3N_2S$	Found
N	13.71	13.64

1-Acetyl-4-methylthiohydantoic Acid, $CH_3CONHCSNHCH(CH_3)COOH$.—From alanine and ethyl acetyldithiocarbamate. Alanine is apparently less reactive than glycocoll and it was necessary to heat with the carbamate for 40 hours before the reaction was complete. The acid is very soluble in hot and cold water. It crystallizes in prisms which melt at 171° to a clear colorless oil, effervescing when heated higher. Analysis (Kjeldahl):

	Calculated for $C_6H_{10}O_3N_2S$	Found
N	14.72	14.36

2-Thio-4-methylhydantoin,  . —1 - Acetyl - 4 - methylthiohydantoic acid was heated with concentrated hydrochloric acid on the steam bath for several hours. After concentration of the solution the methylthiohydantoin was obtained and crystallized from alcohol in flat prisms. The compound melts at 158°–159° to a clear, colorless oil. It is very soluble in boiling alcohol and water. Analysis (Kjeldahl):

	Calculated for $C_4H_6ON_2S$	Found
N	21.53	21.31

NEW HAVEN, CONN.
July 22, 1911

UNSATURATED δ-KETONIC ACIDS

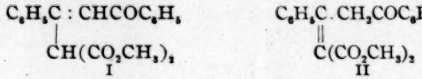
BY E. P. KOHLER

The main object of the following investigation was to study the mode of addition to the conjugated system, C : C.C : O, in cases in which both the addend and the unsaturated chain are parts of the same molecule. Addition in these circumstances necessarily results in some kind of ring formation, hence lactone formation, which generally takes place spontaneously, seemed best adapted for such an investigation. Unsaturated δ-ketonic acids were selected for study because they present the largest number of possibilities, since the lactone ring can close in the β, γ, or δ positions.

The ketonic acids that were used have essentially the same chain that is responsible for the interesting properties of the glutaconic acids. In the course of the investigation it became necessary to compare the two classes of substances and it was found that the properties of the former are quite as remarkable as those of the latter. This part of the work will, however, be reserved for later publication, and the present paper will deal only with the results obtained in the study of lactone formation.

Unsaturated δ-lactonic acids are unknown; but they can be

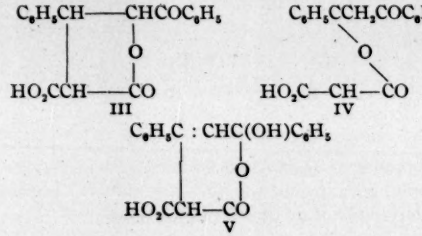
prepared without very great difficulty either by means of the methods used for getting the corresponding saturated compounds, or by introducing bromine into saturated ketonic acids and eliminating hydrobromic acid from the product. Thus when α-brombenzalacetophenone is added to methyl sodiummalonate suspended in ether, one of the products is an unsaturated δ-ketonic ester represented by one of the two following formulas:



I II

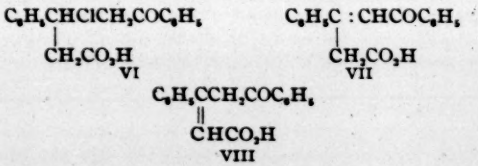
The formation of the ester from α-brombenzalacetophenone, and its behavior on hydrolysis, are most easily interpreted on the assumption that the ethylene linkage is in the position represented by formula I. I shall therefore use this formula; but in view of the ease with which substances of this type undergo isomeric change, and the difficulty of definitely locating the double linkage, this choice must be regarded as provisional.

The ester is rapidly hydrolyzed by alcoholic potassium hydroxide. In the presence of excess of base the product is the expected dipotassium salt, but lactone formation takes place so easily that the corresponding acid cannot be obtained. The dipotassium salt loses base when dissolved in water, and passes into a salt of a monobasic acid that has the composition $C_{18}H_{14}O_5$. For this lactonic acid three formulas are possible, depending upon the way in which the lactone ring is established.

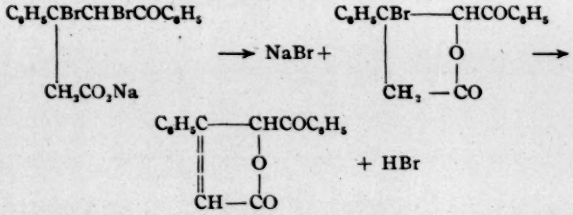


III IV V

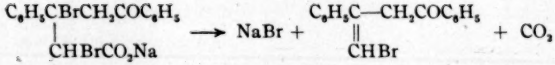
Above 170°, the acid rapidly loses carbon dioxide and passes, in the main, into two products: a saturated lactone melting at 93° and having the composition $C_{17}H_{14}O_2$, and an unsaturated acid isomeric with the lactone. The structure of this unsaturated acid can be deduced from the following transformations: When a solution of the acid in methyl alcohol is saturated with hydrogen chloride, it passes into the methyl ester of a chlor acid that on reduction gives methyl γ-benzyl-β-phenylbutyrate. This shows that no shifting of the groups occurred in the process of heating—the chlorine derivative is methyl benzoylchlorphenylbutyrate (VI), and the acid from which it was obtained must be either benzoylphenylvinylacetic acid (VII) or benzoylphenylcrotonic acid (VIII).



The acid combines with bromine and forms a stable dibromide. The dibromide of benzoylphenylvinylacetic acid would be expected to give either a bromlactone or an unsaturated γ-lactone when dissolved in sodium carbonate:

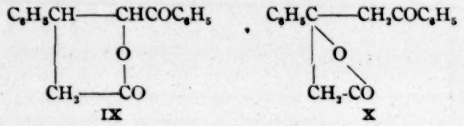


The dibromide of benzoylphenylcrotonic acid, on the other hand, would be expected to give, on similar treatment, a bromine derivative of an unsaturated ketone:

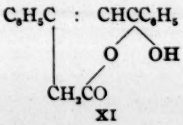


The dibromide of the acid in question readily dissolves in sodium bicarbonate, but the clear solution almost immediately becomes milky owing to the separation of an indifferent bromine compound, and in a very short time this passes quantitatively into an unsaturated lactone. The unsaturated acid is, therefore, benzoylphenylvinylacetic acid, as represented by formula (VII).

Benzoylphenylvinylacetic acid usually forms about 40 per cent. of the product obtained by heating the ketolactonic acid. Its potassium salt is the only substance obtained by dissolving the lactone melting at 93° in alcoholic potassium hydroxide, showing that no shifting of the phenyl and benzoyl groups has occurred during the formation of this lactone. This leaves three possible formulas for the substance:

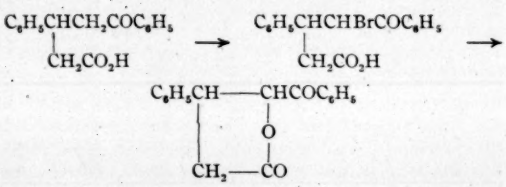


IX X



XI

Benzoylphenylvinylacetic acid could be formed from a lactone having any of these formulas, but it is little likely that an α-hydroxy acid, such as would be obtained by opening the ring in the γ-lactone represented by formula (IX), would so readily lose water and pass into an unsaturated acid. Moreover, the two stereoisomeric lactones having this structure are easily obtained by applying to benzoylphenylbutyric acid the commonest method used for getting γ-lactones:



Both of the substances obtained in this way are different from the lactone in question. This must, therefore, be represented either by (X) or (XI). It was difficult to decide between these formulas because nearly all reagents that attacked the carbonyl group also opened the lactone ring, and any product obtained in this way can be accounted for equally well with either formula. By using great care, however, it was found possible to add ethylmagnesium bromide to the substance and get two stereoisomeric hydroxylactones. This excludes formula (XI), and leaves only that of a β-lactone.

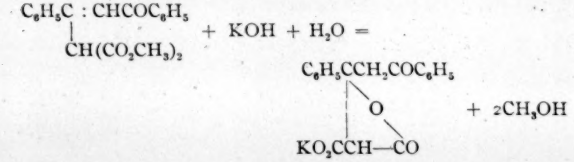
The ease with which the lactone passes into an unsaturated acid is in harmony with this conclusion. The hydroxy acid obtained by opening the ring in a substance represented by formula (X) belongs to the most unstable type of hydroxy acids because it has a tertiary hydroxyl group in the β position and no hydrocarbon residue in the α position with reference to ketonic carbonyl; it therefore readily loses water and passes into an unsaturated acid. This formula, finally, is confirmed by a method of preparation of the lactone that is essentially the same as that which has been used for getting nearly all β-lactones that are known.

When a solution of benzoylphenylvinylacetic acid, in glacial acetic acid, is saturated with hydrogen bromide, the unsaturated acid passes into an exceedingly unstable brom acid in which the bromine must be in the β position:

When the brom acid is dissolved in sodium carbonate it rapidly loses all its bromine; a small part of the product re-

mains in solution as sodium salt of the unsaturated acid, and the rest separates as a lactone identical with the product obtained by heating the ketolactonic acid.

There can be no doubt, therefore, that the lactone melting at 93° is a β-lactone, and that in the ketolactonic acid from which it was obtained by heating the ring is also closed in the β position. The formation of a β-lactone containing a ring that is usually closed with difficulty here takes place so easily that the ester of the dibasic acid is rapidly and completely hydrolyzed by one equivalent of base:



This is the best method for getting the ketolactonic acid. The product obtained in this way appears to be homogeneous, but by very careful recrystallization from absolute ether it is possible to separate it into two isomeric acids, the one already considered and which constitutes at least 98 per cent. of the whole, and another that gives the same products with nearly all reagents but crystallizes in a different form and gives a lactone melting at 124° when heated.

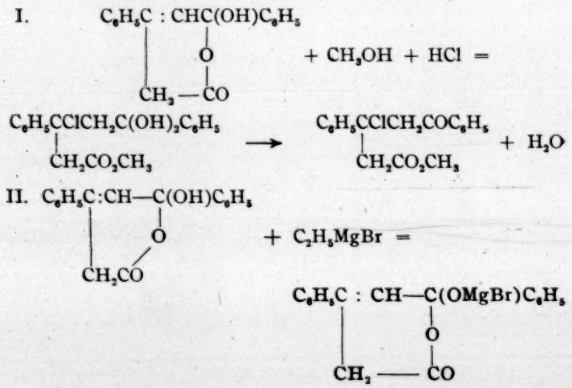
The lactone melting at 124° was obtained in very small quantity only, but its structure is established by the following transformations:

1. The substance, like the isomeric lactone melting at 93°, gives benzoylphenylchlorbutyric ester when its solution in alcohol is saturated with hydrogen chloride.

2. When the ring is opened by solution in alcoholic potassium hydroxide, the result is the potassium salt of the same unsaturated acid that is obtained from the isomeric lactone.

3. With ethylmagnesium bromide the first product is a magnesium derivative from which acids regenerate the lactone; it is not possible to add the reagent without opening the ring.

These facts show that the substance melting at 124° is the hydroxylactone represented by formula (XI), the typical reactions being represented by the following equations:



The second lactonic acid obtained by hydrolyzing benzoylphenyvinylmalonic ester is, therefore, the δ-lactonic acid represented by formula (V). The formation of a β- and a δ-lactone from the unsaturated ketonic acid, when all other unsaturated acids give γ-lactones, shows that ring formation in this case is determined entirely by the properties of the conjugated system C : C . C : O. The β-lactone is the result of 1,4-addition, the δ-lactone that of 1,2-addition to this system, and it is clear that in addition reactions in which both addend and unsaturated chain are a part of the same molecule, the mode of addition is the same as in those in which they are brought together as separate compounds.

EXPERIMENTAL PART

In the first experiments sodium alcoholate was added in small quantities to an alcoholic or ethereal solution containing equivalent amounts of α-brombenzalacetophenone and ethyl malonate. The solution assumed a bright red color

and sodium bromide began to separate almost immediately. The addition of alcoholate was continued until the mixture remained alkaline for an hour. The solution yielded no solid product, but by boiling it with alcoholic potassium hydroxide it was possible to get the dipotassium salt of benzoylphenylvinylmalonic acid, showing that condensation had taken place in the desired direction.

Methyl malonate was then substituted for the ethyl ester in the hope of getting a solid product and the reaction was carried out with the sodium derivative suspended in absolute ether. Some solid methyl ester of the unsaturated ketonic acid was obtained in this way, but the method is not satisfactory. In order to complete the reaction it is necessary to use much more than one equivalent of the sodium derivative and to boil for hours. It is difficult, therefore, to determine when the reaction is complete and the protracted boiling leads to the formation of by-products that seriously interfere with the isolation of the ester. The yield of dipotassium salt obtained by hydrolyzing the entire product was 60–70 per cent., that of pure solid ester small.

Much better results were obtained by starting with the corresponding saturated ketonic ester. Vorländer[1] showed that, under the influence of sodium alcoholate, malonic ester readily combines with benzalacetophenone both in ethereal and alcoholic solution. He did not, however, isolate the addition product, but hydrolyzed it and analyzed the resulting acid. I found that the amount of pure ester obtainable by this method is small and that even when sodium malonate and absolute ether are used the yields both of pure ester and of acid are unsatisfactory.

Excellent results were obtained, however, by using piperidine in place of sodium alcoholate as condensing agent. The procedure is shown by the following experiment: Ten grams of piperidine were added to a solution of 208 grams of benzalacetophenone and 140 grams of methyl malonate in 400 cc. of methyl alcohol. The mixture was boiled continuously for 72 hours, then distilled until most of the alcohol was re-

[1] Ann. Chem. (Liebig), **294**, 332.

moved, and the residue allowed to cool. The solid was transferred to a Buchner funnel and thoroughly washed with well-cooled methyl alcohol. One recrystallization from methyl alcohol gave 244 grams of the pure methyl ester described in a previous paper[1]—a yield of about 80 per cent. The filtrates were combined, the solvent removed by distillation and the piperidine by washing with acid, but the residue only partially solidified. It was therefore hydrolyzed. It gave 30 grams of pure acid, making a total yield of over 90 per cent.

Ethyl γ-benzoyl-β-phenylethylmalonate, $C_6H_5CHCH_2COC_6H_5$, $CH(CO_2C_2H_5)_2$ was obtained both by direct condensation and by saturating an alcoholic solution of the acid with hydrogen chloride. It was purified by recrystallization from alcohol, from which it separates in friable needles melting at 65°. It is readily soluble in all common organic solvents except ligroin and crystallizes poorly from all.

Analysis:

0.1422 gram substance gave 0.3730 gram CO_2 and 0.0861 gram H_2O.

	Calculated for $C_{22}H_{24}O_5$	Found
C	71.9	71.5
H	6.5	6.7

The esters of benzoylphenylmalonic acid have two hydrogen atoms that are replaceable with bromine; but, as was expected, one of these is much more easily replaced than the other because substituents diminish the mobility of hydrogen in malonic esters. The introduction of bromine was carried out in chloroform or carbon tetrachloride. The reaction commenced slowly at the ordinary temperature, but after it was well started the bromine disappeared as fast as it was added until the solution contained a molecule of halogen per molecule of ester. The solvent was then removed by distillation under diminished pressure and the residue poured into methyl alcohol.

[1] THIS JOURNAL, **46**, 234.

Both the ethyl and methyl esters gave isomeric bromine compounds. That these are not structural isomers is shown by the fact that both form the same unsaturated ester when hydrogen bromide is eliminated by means of reagents which, like diethylaniline, do not cause isomeric change. They are, therefore, stereoisomers—possible because the substances contain two dissimilar asymmetric carbon atoms.

Ethyl γ-Benzoyl-γ-brom-β-phenylethylmalonate, $C_6H_5CHCHBrCOC_6H_5$ / $CH(CO_2C_2H_5)_2$.—The products from the ethyl ester were separated with difficulty. The methyl alcoholic solution first deposited needles that, after purification, melted at 88°. The filtrates, on evaporation, left an oil that solidified in the course of a few weeks, and the resulting solid was finally separated by means of ether-ligroin mixtures. It yields some more of the needles melting at 88° and a new substance melting at 43° and crystallizing in large prisms or tables.

Analysis:

I. 0.1586 gram substance (88°) gave 0.3438 gram CO_2 and 0.0745 gram H_2O.

II. 0.1762 gram substance (43°) gave 0.3835 gram CO_2 and 0.0821 gram H_2O.

	Calculated for $C_{22}H_{23}O_5Br$	Found I	Found II
C	59.1	59.2	59.4
H	5.1	5.2	5.2

The two isomeric bromine compounds obtained from the methyl ester of benzoylphenylethylmalonic acid were easily separated by crystallization from methyl alcohol. One crystallizes in needles melting at 113°, the other in plates or prisms melting at 87°. Both are moderately soluble in cold alcohol and ether, sparingly in ligroin.

Analysis:

I. 0.1525 gram substance (113°) gave 0.3227 gram CO_2 and 0.0618 gram H_2O.

II. 0.1681 gram substance (87°) gave 0.3550 gram CO_2 and 0.0679 gram H_2O.

	Calculated for $C_{20}H_{19}O_5Br$	Found I	Found II
C	57.3	57.7	57.6
H	4.4	4.5	4.5

Methyl γ-Benzoyl-α,γ-dibrom-β-phenylethylmalonate, $C_6H_5CHCHBrCOC_6H_5$ / $CBr(CO_2CH_3)_2$.—The second reactive hydrogen atom in benzoylphenylethylmalonic esters can be replaced both by boiling solutions of the monobrom substitution products, in carbon tetrachloride, with bromine, and by exposing the solutions to the action of direct sunlight for a long time. The methyl ester yielded two isomeric products that were separated by crystallization from alcohol. The less soluble compound separated in needles melting at 132°, while the second product crystallized in large tables melting at 94°.

Analysis:

I. 0.1206 gram substance (132°) gave 0.2110 gram CO_2 and 0.0390 gram H_2O.

II. 0.1608 gram substance (94°) gave 0.2825 gram CO_2 and 0.0520 gram H_2O.

	Calculated for $C_{20}H_{18}O_5Br_2$	Found I	Found II
C	48.2	47.7	47.9
H	3.6	3.6	3.6

Methyl γ-Benzoyl-β-phenylvinylmalonate, $C_6H_5C:CHCOC_6H_5$ / $CH(CO_2CH_3)_2$.—Although the monobrom substitution products of benzoylphenylethylmalonic esters lose hydrobromic acid with the greatest ease, it is, nevertheless, difficult to get a satisfactory yield of pure unsaturated ester. The difficulty is two-fold: the unsaturated esters very readily undergo isomeric change under the influence of nearly all reagents that can be used for eliminating the halogen acid; and small quantities of impurities greatly interfere with the separation of the esters in solid form. After trying many reagents under various conditions the following procedure was finally adopted as the most satisfactory.

A 10 per cent. solution of potassium hydroxide in equal parts of methyl alcohol and water is added, in small quantities, to a boiling solution of the ester in 4 times its weight of the same alcohol. Every addition of base produces a faint yellow color that immediately disappears on shaking. The reaction is complete when the yellow color and an alkaline reaction remain after vigorous shaking for a minute. The methyl alcohol is then removed by distillation, the residue extracted with ether, and the ethereal solution washed with water until free from alcohol. The addition of a few crystals of ester to the dried ethereal solution induces the separation of a large part of the ester in almost pure form, and the amount may be increased by judicious addition of ligroin to the solution. In the absence of "seed" it is necessary to allow the solvent to evaporate and await spontaneous crystallization in the resultant oil. This generally takes several weeks and may take months.

The yield of pure solid ester obtainable in this way is 60–70 per cent. The amount may be increased, somewhat, by manipulating the filtrates, but it is more economical to boil these with alcoholic potassium hydroxide and isolate the resulting acid. The total yield is 85–90 per cent.

The ester is readily soluble in common organic solvents except ligroin. It separates from ether in small flat needles, from methyl alcohol in large transparent prisms or tables. Its melting point is 94°.

Analysis:

0.1383 gram substance gave 0.3590 gram CO_2 and 0.0700 gram H_2O.

	Calculated for $C_{20}H_{18}O_5$	Found
C	71.0	70.8
H	5.4	5.6

Methyl benzoylphenylvinylmalonate immediately reduces a cold solution of potassium permanganate in acetone, but apparently does not combine with bromine. No reaction takes place when bromine is added to its solution in carbon tetrachloride at the ordinary temperature and in diffuse

daylight. When the solution is warmed or exposed to direct sunlight, the bromine slowly disappears but the reaction is accompanied by evolution of hydrobromic acid and the resulting solid is a monosubstitution product. This was purified by crystallization from alcohol. It separated in prisms or tables melting at 141°.

Analysis:

0.1622 gram substance gave 0.3434 gram CO_2 and 0.0613 gram H_2O.

	Calculated for $C_{20}H_{17}O_3Br$	Found
C	57.6	57.7
H	4.1	4.2

As it is impossible to determine whether the substance is formed by direct replacement, or by addition followed by loss of hydrogen bromide, the location both of the bromine and of the ethylene linkage is uncertain.

Hydrolysis of Methyl Benzoylphenylvinylmalonate.—As stated in the introduction, the pure ester can be hydrolyzed without loss by using exactly 1 equivalent of potassium hydroxide. For this purpose the ester is dissolved in 5 times its weight of alcohol that has been distilled from solid potassium hydroxide. The base is added as a 25 per cent. solution in equal parts of alcohol and water. The solution becomes neutral on standing for 10–12 hours in an ice chest, and most of the resulting potassium salt separates in long, colorless needles. These were washed with a small quantity of cooled acetone and analyzed.

0.3110 gram substance gave 0.1101 gram K_2SO_4.

	Calculated for $C_{18}H_{13}O_5K$	Found
K	15.72	15.6

For hydrolyzing the impure ester obtained from residues it is better to use a large excess of base because it is possible to get rid of impurities by washing the dipotassium salt, which is sparingly soluble in excess of strong potassium hydroxide. The procedure is as follows: Aqueous potassium hydroxide (2 : 3) is added in large excess to an alcoholic

solution of the ester. The mixture is well shaken and allowed to stand in an ice chest for 10–12 hours. The resulting yellow or orange liquid is then slowly concentrated on a water bath until most of the potassium salt has separated. The liquid is filtered and the salt repeatedly washed with cold acetone. Unless the ester contained very large quantities of impurities the result is a colorless salt crystallizing in small, thin plates. An analysis of the air-dried salt gave the following results:

I. 0.4225 gram salt lost 0.0363 gram at 120°.
II. 0.6110 gram salt lost 0.0397 gram at 120°.

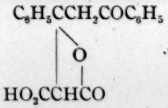
	Calculated for $C_{18}H_{12}O_5K_2.2H_2O$	Found I	Found II
H_2O	8.53	8.6	8.65

0.3862 gram anhydrous salt gave 0.1741 gram K_2SO_4.

	Calculated for $C_{18}H_{12}O_5K_2$	Found
K	20.21	20.2

The salt is stable in ordinary air, but on extremely damp summer days it deliquesces and passes into hydrogen potassium carbonate and the monopotassium salt previously described. The same salt separates when a mixture of alcohol and ether is added to the strongly alkaline water solution of the dipotassium salt.

Benzoylphenylbutyrolactonic Acid,



.—From solutions of either of the potassium salts obtained by hydrolyzing methyl benzoylphenylvinylmalonate acids precipitate a colorless oil that slowly solidifies. The only solvents from which the resulting solid can be obtained in well-defined crystals are water and ether. It is sparingly soluble in boiling water and separates very slowly and incompletely on cooling the solution. In ether it is so readily soluble that only large quantities or comparatively pure preparations can be recrystallized from it with advantage.

The acid separates from water in small, lustrous pyramids containing 2 molecules of water of crystallization, which it loses below 100°.

I. 1.1066 grams substance, dried on paper, lost 0.1196 gram at 80° to 105°.

II. 1.7707 grams substance, air-dried, lost 0.1871 gram at 80° to 105°.

	Calculated for $C_{18}H_{14}O_5.2H_2O$	Found I	Found II
H_2O	10.4	10.8	10.5

When heated slowly, the hydrous acid melts at about 100°, then loses water and resolidifies, and finally melts with decomposition at about 170°. The acid separates from ether in translucent plates that begin to decompose at the same temperature as the dehydrated acid crystallized from water.

Analysis:

I. 0.1400 gram substance (dehydrated) gave 0.3550 gram CO_2 and 0.0606 gram H_2O.

II. 0.1404 gram substance (from ether) gave 0.3577 gram CO_2 and 0.0581 gram H_2O.

	Calculated for $C_{18}H_{14}O_5$	Found I	Found II
C	69.7	69.2	69.5
H	4.5	4.8	4.6

Diphenylhydroxycrotolactonic Acid, $C_6H_5C : CH—C(OH)C_6H_5$ / $HO_2CCHCO—O$.—The product of hydrolysis of the unsaturated ester contained a small quantity of a second acid that accumulated in the ethereal filtrate. This acid could be isolated only from the unusually pure preparations obtained by hydrolyzing with one equivalent of base, and from these only when large quantities were hydrolyzed at a time. It crystallizes in fine needles that are extremely soluble in ether, are decomposed by boiling water, and are apparently changed when exposed in an impure state to air or light.

When heated rapidly, the substance melts with decomposition at about 170°.

Analysis:

0.1544 gram substance gave 0.3935 gram CO_2 and 0.0639 gram H_2O.

	Calculated for $C_{18}H_{14}O_5$	Found
C	69.7	69.5
H	4.5	4.6

γ-Benzoyl-β-phenylvinylacetic Acid, $\begin{matrix} C_6H_5C : CHCOC_6H_5 \\ | \\ CH_2CO_2H \end{matrix}$.—The product obtained by heating the ketolactonic acid contained at least 4 substances, 2 of which were acid, the remainder indifferent. The acids were isolated as follows: The lactonic acid was heated to 170°–185° in an oil bath until the evolution of carbon dioxide ceased. The amber-yellow liquid, while still hot, was poured into ether in a separating funnel and the solution extracted with sodium carbonate until free from acid. From the solution in sodium carbonate acids precipitated an oil that soon solidified. The solid was washed, dried and crystallized from ether or ether-ligroin mixtures. From 95 to 98 per cent. of the acid product consists of an acid which separates in small colorless prisms that melt at 135°.

Analysis:

0.1128 gram substance gave 0.3171 gram CO_2 and 0.0542 gram H_2O.

	Calculated for $C_{17}H_{14}O_3$	Found
C	76.7	76.6
H	5.3	5.4

Benzoylphenylvinylacetic acid liquefies in contact with alcohol and acetone, is sparingly soluble in carbon tetrachloride and ligroin, insoluble in water. In ether it is moderately soluble, but both dissolves and separates very slowly. The acid immediately reduces permanganate and combines readily with bromine and halogen acids. An attempt was made to determine the character of the chain by reduction to ben-

zoylphenylbutyric acid, but it was impossible to confine the action of the reducing agent to the ethylene linkage. The acid was therefore transformed into

Methyl γ-benzoyl-β-chlor-β-phenylbutyrate, $C_6H_5CClCH_2COC_6H_5$, $CH_2CO_2CH_3$ by saturatimg its solution in methyl alcohol with hydrogen chloride and purifying the product from alcohol.

Analysis:

0.1325 gram substance gave 0.3330 gram CO_2 and 0.0636 gram H_2O.

	Calculated for $C_{18}H_{17}O_3Cl$	Found
C	68.2	68.6
H	5.4	5.3

The ester is moderately soluble in alcohol and ether. It crystallizes in fine needles melting at 131°. By boiling with zinc dust and methyl alcohol it was possible to eliminate the halogen without attacking the carbonyl group. The product was the methyl ester of benzoylphenylbutyric acid, identified by comparison with a specimen on hand. This result proves that the high temperature used in decomposing the ketolactonic acid did not lead to any shifting of the groups.

γ-Benzoyl-β-phenyl-β,γ-dibrombutyric Acid, $C_6H_5CBrCHBrCOC_6H_5$ CH_2CO_2H.—The addition of bromine to the unsaturated acid was carried out in carbon tetrachloride. In diffuse daylight combination takes place very slowly; it can be greatly accelerated by addition of a little iodine and exposure to direct sunlight. It results in two stereoisomeric products. One of these is very sparingly soluble in carbon tetrachloride and separates almost completely when the solution is cooled in a freezing mixture. It was washed with cold tetrachloride and recrystallized from ethyl acetate or acetone. From these solvents it separates in large colorless plates that decompose below the melting point.

The carbon tetrachloride filtrates, on evaporation, deposi-

ted fine needles that were readily soluble in all solvents except ligroin, but could be purified by recrystallization from alcohol-free ether. This substance also decomposes below its melting point.

Analysis:

I. 0.1455 gram substance (plates) gave 0.2571 gram CO_2 and 0.0440 gram H_2O.

II. 0.1600 gram substance (needles) gave 0.2820 gram CO_2 and 0.0482 gram, H_2O.

	Calculated for $C_{17}H_{14}O_3Br_2$	Found I	Found II
C	47.9	48.2	48.1
H	3.3	3.3	3.3

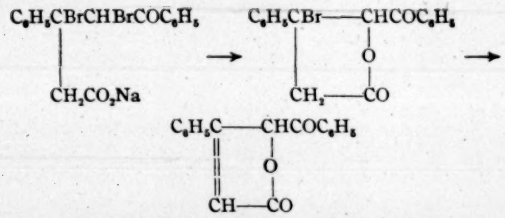
The two bromine compounds behave in the same way when they are added to a solution of sodium bicarbonate and they give the same product. If they are added as a sufficiently fine powder they dissolve rapidly and form a clear solution. This shortly becomes milky, owing to the separation of a bromine compound. All efforts to isolate this failed because it loses hydrogen bromide so easily that before the extremely finely divided material can be filtered most of it passes into an unsaturated lactone. This was easily purified by crystallization from alcohol. It crystallizes in colorless or very pale yellow needles that melt at 131°.

Analysis:

0.1322 gram substance gave 0.3760 gram CO_2 and 0.0540 gram H_2O.

	Calculated for $C_{17}H_{12}O_3$	Found
C	77.2	76.9
H	4.6	4.5

The lactone is insoluble in sodium carbonate but dissolves readily in alcoholic potassium hydroxide. From the bright red solution acids reprecipitate the lactone. It is therefore probably a γ-lactone, and as its formation is preceded by that of an intermediate bromine compound, the reaction probably takes place in the following steps:



The formation of any unsaturated lactone in this reaction establishes the position of the bromine atoms, and therefore that of the double linkage in the unsaturated acid.

The mother liquors from benzoylphenylvinylacetic acid, on standing, deposited a small quantity of a second acid that is much less soluble, crystallizes in large plates, and melts at 180°.

Analysis:

0.1375 gram substance gave 0.3842 gram CO_2 and 0.0643 gram H_2O.

	Calculated for $C_{17}H_{14}O_3$	Found
C	76.7	76.2
H	5.3	5.2

The acid is isomeric with the unsaturated acid just described. It immediately reduces permanganate but does not combine with bromine. Its solution in sodium carbonate is colorless while that in strong potassium hydroxide is yellow. The acid is evidently not a geometrical isomer of the acid melting at 135°. It is obtained in very small amounts as it constitutes less than half a per cent of the acid products.

The ethereal solution from which the acids were extracted with sodium carbonate contained two lactones. One of these is colorless, readily soluble in alcohol, moderately soluble in ether; the other is lemon-yellow, readily soluble in ether, moderately in alcohol. By adding ligroin to the dried ethereal solution and cooling in a freezing mixture it was possible to precipitate most of the colorless lactone. This was filtered, washed with cooled ether until colorless and recrystallized

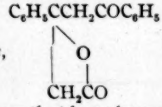
from alcohol. It separates from hot solutions in needles, from cold solutions in stout prisms or tables melting at 93°.

Analysis:

0.1304 gram substance gave 0.3660 gram CO_2 and 0.0650 gram H_2O.

	Calculated for $C_{17}H_{14}O_3$	Found
C	76.7	76.6
H	5.3	5.5

As shown in the introduction, this substance is

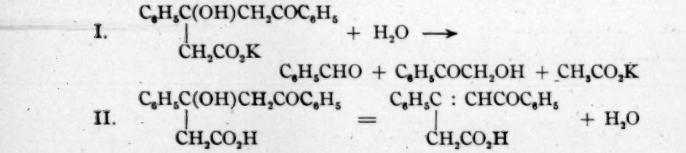
γ-Benzoyl-β-phenyl-β-butyrolactone,  . It is

much more stable than the β-lactones that have been described heretofore; it is not affected by boiling either with water or sodium carbonate and it can be heated to 200° without change. Even above this temperature it does not, like most other β-lactones, lose carbon dioxide but instead undergoes a complex decomposition.

The lactone ring is easily opened by solution in alcoholic potassium hydroxide. If the lactone is added to the well-cooled alkaline solution in the form of a very fine powder, and the liquid is acidified as soon as all is in solution, the sole product is benzoylphenylvinylacetic acid. If the alkaline solution is allowed to stand for some time before acidification, the product may contain a considerable quantity of indifferent substances. For the purpose of isolating these, 25 grams of lactone were dissolved in an excess of cold alcoholic potash and the solution allowed to stand in an ice chest overnight. The solution was then poured into water and the indifferent products extracted with ether. The ether, on distillation, left 8.4 grams of colorless oil that was fractioned under diminished pressure. It was thus separated into almost equal parts of benzaldehyde, recognized by the odor, and benzoylcarbinol, identified by its boiling point and by comparison with a specimen made from ω-bromacetophenone.

The formation of these substances indicates that when the

lactone ring is opened the first product is, as usual, the salt of a hydroxy acid, and that this decomposes in the alkaline solution while the corresponding acid more easily loses water:



The lactone ring is also easily opened with acids. When the methyl alcoholic solution is saturated with hydrogen chloride and then allowed to stand for several days, the lactone passes completely into the ester of benzoylphenylchlorbutyric acid that was described above. Similarly, when the solution of the lactone in glacial acetic acid was saturated with hydrogen bromide the principal product was

γ-Benzoyl-β-phenyl-β-brombutyric Acid, $C_6H_5CBrCH_2COC_6H_5$ / CH_2CO_2H.—

This extremely unstable acid was isolated as follows. The solution was allowed to stand in an ice chest for a week after it had been saturated with hydrogen bromide. It was then poured into the ice water and shaken with enough benzene to dissolve all of the yellow oil that separated. The benzene solution was repeatedly washed with ice water, then dried and the benzene evaporated in a current of dry air, under diminished pressure. The residue consisted of crystals imbedded in a yellow oil. The oil was absorbed in a porous plate and the solid washed, on the plate, with small quantities of cold, alcohol-free ether until it was almost colorless. It was then recrystallized from absolute ether, from which it separated in long colorless needles that decomposed without melting.

Analysis:

0.1505 gram substance gave 0.3267 gram CO_2 and 0.0624 gram H_2O.

	Calculated for $C_{17}H_{15}O_3Br$	Found
C	58.8	59.2
H	4.3	4.5

The same acid was obtained by dissolving benzoylphenylvinylacetic acid in glacial acetic acid, saturating the solution with hydrogen bromide and treating the solution as before. This method of preparation proves that the bromine is in the β position. For even if the double linkage in the unsaturated acid had shifted, the result of the addition of hydrogen bromide would still necessarily be a β-brom derivative.

The acid is readily soluble in sodium carbonate but the solution remains clear for but a few minutes. The faint milkiness that appears at first soon changes to a mass of needles that continue to grow for several hours. The needles are identical with the product obtained by heating the ketolactonic acid, thus proving, conclusively, that in this lactone and in the ketolactonic acid from which it is obtained the lactone rings are closed in the β position. The only other product formed by the action of sodium carbonate on the brom acid is a small quantity of benzoylphenylvinylacetic acid.

δ-Hydroxy-β,δ-diphenyl-β-heptalactone, $C_6H_5CCH_2C(C_2H_5)(C_6H_5)$ (with O and CH_2COOH) .—When an ethereal solution of the lactone melting at 93° is added to ethylmagnesium bromide at the ordinary temperature the resulting reaction involves both the carbonyl group and the lactone ring—the product is insoluble in alcoholic potassium hydroxide. By adding the lactone in the form of a fine powder and keeping the reagent in a freezing mixture it is possible to confine the action to the carbonyl group. The final result in this case depends upon the subsequent treatment of the magnesium compound. When this is decomposed with ice water before addition of acid, the product is a substance that crystallizes in thick needles melting at 190°. When, on the other hand, the magnesium derivative is poured directly into a mixture of ice and concentrated hydrochloric acid, the product crystallizes in fine needles melting at 140°. Both substances were purified by crystallization from methyl alcohol.

Analysis:

I. 0.1291 gram substance (190°) gave 0.3655 gram CO_2 and 0.0804 gram H_2O.

II. 0.1420 gram substance (140°) gave 0.4030 gram CO_2 and 0.0880 gram H_2O.

	Calculated for $C_{19}H_{20}O_3$	Found I	Found II
C	77.0	77.2	77.4
H	6.8	6.9	6.9

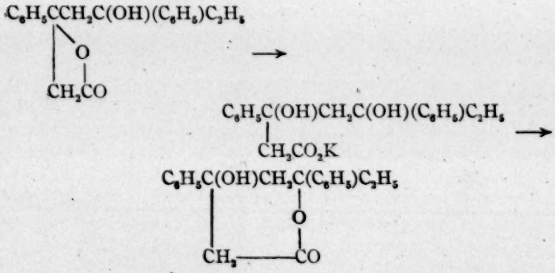
These substances are stereoisomeric lactones. They are insoluble in sodium carbonate, soluble in alcoholic potassium hydroxide. From solutions of the potassium salts obtained from both, acids precipitate a third isomeric lactone that melts at 150°. This was likewise purified by crystallization from methyl alcohol, from which it separates in large lustrous needles.

Analysis:

0.1560 gram substance gave 0.4380 gram CO_2 and 0.0960 gram H_2O.

	Calculated for $C_{19}H_{20}O_3$	Found
C	77.0	77.0
H	6.8	6.8

As only 2 stereoisomeric β-lactones are possible, this third substance must be a δ-lactone. Its formation from an acid that has tertiary hydroxyl groups in both the β and δ positions, and similar residues in combination with the carbon atoms that hold the hydroxyl groups, is good evidence that the lactone ring closes more readily in the δ than in the β position.



The yellow lactone contained in small quantity in the filtrates from benzoylphenylbutyrolactone was purified with great difficulty. It does not crystallize from ether and it is so sensitive that it is changed even by boiling with alcohol. It was therefore dissolved in ether and this solution poured into ten times its volume of hot alcohol. After several repetitions of this process it was obtained in thin lemon-yellow plates that melted sharply at 172°.

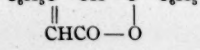
Analysis:

0.1403 gram substance gave 0.4215 gram CO_2 and 0.0632 gram H_2O.

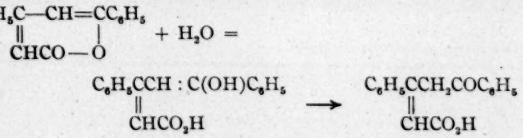
0.1106 gram substance gave 0.3325 gram CO_2 and 0.0500 gram H_2O.

	Calculated for $C_{17}H_{12}O_2$	Found I	Found II
C	82.3	81.9	82.0
H	4.9	5.0	5.0

The substance is insoluble in sodium carbonate. From its solution in alcoholic potassium hydroxide acids precipitate the unsaturated acid melting at 180°. The yellow substance is evidently, therefore, an unsaturated lactone. Since acids neither precipitate a hydroxy acid nor regenerate the lactone from the potassium salt, it probably is not a γ-lactone. The ketolactonic acid could not yield an unsaturated β-lactone without a shifting of the phenyl group. The most probable formula for the yellow substance is therefore



This formula accounts for the color, the instability, and the formation of an unsaturated acid, isomeric with benzoylphenylvinylacetic acid, when the ring is opened.



δ-Hydroxy-β,δ-diphenyl-δ-crotolactone,

$C_6H_5C = CHC(OH)C_6H_5$
$\quad\quad\quad

starting point was the corresponding saturated ketonic acid, prepared as directed by Vorländer.[1]

γ-Benzoyl-γ-brom-β-phenylbutyric Acid, $C_6H_5CHCHBrCOC_6H_5$ / CH_2CO_2H.—Benzoylphenylbutyric acid is sparingly soluble both in chloroform and in carbon tetrachloride but it reacts so readily with bromine that it is not necessary to dissolve it. In working with large quantities it is better to suspend the finely powdered acid in a moderate quantity of nearly boiling carbon tetrachloride, add a little bromine and await the initial reaction. After that, bromine may be added freely until the color no longer disappears. Much of the product separates in crystalline form in the course of the reaction and most of the remainder is deposited when the solution is cooled in a freezing mixture. The solid that separates from the boiling solution consists largely of an acid that melts with decomposition at about 189°, while most of that which is deposited from the cooled solution consists of an isomeric acid melting and decomposing at about 145°. Both products were recrystallized from ethyl acetate. The higher melting acid separates in large flat needles or plates, the lower melting in small prisms.

Analysis:

I. 0.1660 gram substance (189°) gave 0.3601 gram CO_2 and 0.0692 gram H_2O.

II. 0.1675 gram substance (145°) gave 0.3615 gram CO_2 and 0.0685 gram H_2O.

	Calculated for $C_{17}H_{15}O_3Br$	Found I	Found II
C	58.8	59.1	58.8
H	4.3	4.6	4.6

The two stereoisomeric methyl esters corresponding to these acids were obtained both by introducing bromine into methyl benzoylphenylbutyrate and by saturating solutions of the brom acids in methyl alcohol with hydrogen chloride. They were separated by recrystallization from methyl alcohol.

[1] Ann. Chem. (Liebig), **294**, 332.

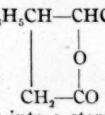
One crystallizes in needles melting at 132°, the other in prisms melting at 87°.

Analysis:

I. 0.1404 gram substance (132°) gave 0.3063 gram CO_2 and 0.0634 gram H_2O.

II. 0.1775 gram substance (87°) gave 0.3835 gram CO_2 and 0.0787 gram H_2O.

	Calculated for $C_{18}H_{17}O_3Br$	Found I	Found II
C	59.3	59.5	59.6
H	4.7	5.0	4.9

γ-Benzoyl-β-phenyl-γ-butyrolactone,  .—

Each of the γ-brom acids rapidly passes into 2 stereoisomeric lactones when dissolved in sodium carbonate. These were separated by crystallization from methyl alcohol. The principal product (80 per cent.) crystallizes in large tables melting at 130°, the other (18 per cent.) separates in lustrous needles melting at 98°. Both are readily soluble in alcohol and ether.

Analysis:

I. 0.1328 gram substance (130°) gave 0.3725 gram CO_2 and 0.0625 gram H_2O.

II. 0.1205 gram substance (98°) gave 0.3370 gram CO_2 and 0.0585 gram H_2O.

	Calculated for $C_{17}H_{14}O_3$	Found I	Found II
C	76.7	76.5	76.3
H	5.3	5.3	5.4

The same lactones are obtained when either the brom acids or their methyl esters are heated with dimethylaniline to the boiling point of the solvent. The quantitative relations are, however, reversed, the product obtained at the high temperature being composed mainly of the lower-melting lactone. Some of this lactone is formed when the acid is heated by itself, but it is mixed with a large quantity of by-products. When the lactones are obtained by these high-

temperature reactions they are formed directly from the bromine compound and not from an intermediate unsaturated compound, because the unsaturated ketonic acid obtained by eliminating hydrogen bromide from the γ-brom acid gives only the β-lactone when heated with dimethylaniline.

γ-Benzoyl-γ-hydroxy-β-phenylbutyric Acid, $C_6H_5CHCH(OH)COC_6H_5$ (with CH_2CO_2H below the first CH).—The hydroxy acid was obtained from both of the lactones by solution in alcoholic potassium hydroxide and subsequent acidification. It is unstable both in the presence of bases and of acids. In alkaline solution it probably behaves like other α-hydroxy ketones, as one of the products identified was benzoylphenylbutyric acid:

$$2C_6H_5CHCH(OH)COC_6H_5 \;(CH_2CO_2K) = C_6H_5CHCH_2COC_6H_5 \;(CH_2CO_2K) + C_6H_5CHCOCOC_6H_5 \;(CH_2CO_2K) + H_2O$$

In the presence of acids, the substance rapidly reverts to the lactone. The pure acid was obtained as follows:

An ethereal solution of the lactone was shaken with strong cold sodium hydroxide until further addition of the base no longer increased the amount of crystalline sodium salt that separated. The salt was immediately filtered off and washed with alcohol. The washed salt was dissolved in ice water and cautiously acidified with cold dilute hydrochloric acid. This precipitated a colorless solid which was removed as quickly as possible and washed thoroughly with water. The wet acid was dissolved in ether, the solution dried, filtered and diluted with petroleum ether. The acid separated in long colorless needles that melted, with decomposition, at 160°.

Analysis:

0.1480 gram substance gave 0.3909 gram CO_2 and 0.0730 gram H_2O.

	Calculated for $C_{17}H_{16}O_4$	Found
C	71.8	72.0
H	5.6	5.5

When the acid is allowed to remain in contact with dilute acids it rapidly passes into the high-melting lactone; above the melting point it loses water rapidly and gives the low-melting lactone, which is evidently the only form that is stable at high temperatures.

γ-Benzoyl-γ-hydroxy-β-phenyl-γ-heptalactone, $C_6H_5CHCHC(OH)(C_2H_5)C_6H_5$, was one of the products obtained by the action of ethylmagnesium bromide on the high-melting lactone. It was purified by crystallization from methyl alcohol, from which it separates in needles melting at 103°.

Analysis:

0.1412 gram substance gave 0.3974 gram CO_2 and 0.0865 gram H_2O.

	Calculated for $C_{19}H_{20}O_3$	Found
C	77.0	76.7
H	6.8	6.8

The substance is not attacked by boiling sodium carbonate and it is reprecipitated when its solution in alcoholic potassium hydroxide is acidified.

It is much more difficult to confine the action of the Grignard reagent to the carbonyl group in the case of this γ-lactone than in that of the corresponding β-lactone. The procedure was exactly the same with both, but the γ-lactone always yielded a considerable quantity of material that was insoluble in alcoholic potassium hydroxide.

CHEMICAL LABORATORY
BRYN MAWR COLLEGE

THE BROMINATION OF PHENOL

BY J. G. DINWIDDIE AND J. H. KASTLE

It is an interesting fact that when bromine is added to an aqueous solution of phenol only tribromphenol and tribromphenol bromide, tetrabromcyclohexadienone, are formed. No one has ever obtained any evidence of the formation of lower

substitution products. In the course of some work with phenol it was observed by one of us, Kastle, that bromine acts readily upon phenol in such organic solvents as glacial acetic acid and chloroform, with the formation of colorless substitution products and the evolution of hydrobromic acid gas. It therefore occurred to him that it might be of interest to determine just what substitution products of phenol were produced under these conditions. Accordingly it was suggested to Mr. Dinwiddie to undertake a few experiments with this end in view. The experimental results given in the following are his. Four solvents were employed, namely, glacial acetic acid, chloroform, carbon tetrachloride and carbon bisulphide. In all of the experiments a 1 per cent. solution of phenol in the several solvents and about a 3 per cent. solution of bromine were used, the precise concentration of the bromine being accurately determined in each case. A measured quantity of the phenol solution, in all experiments 5 cc., was placed in a dry glass-stoppered bottle and to this an excess of bromine in the given solvent was added. The mixture was then allowed to stand for different intervals of time at the end of which the bromine remaining was determined by adding a measured quantity of the solution to a strong aqueous solution of potassium iodide, and titrating with 0.1 N sodium thiosulphate, 1 cc. of which was found to be equivalent to 0.00799 gram bromine.

The results of these determinations are given in Table I.

The calculated amounts of bromine required to convert 0.05 gram of phenol into the mono-, di- and tribromphenols, respectively, are 0.08511, 0.1702 and 0.2553 gram. It is evident, therefore, that in the organic solvents thus far investigated the bromination of phenol results in the formation of a dibromphenol or a mixture of the mono- and tribromphenols.

In order to get some further idea of the nature of the bromine substitution product produced by the action of bromine on phenol in these organic solvents, 0.5 gram of phenol was dissolved in 10 cc. of chloroform and to this solution there was added the required amount of bromine to form the dibrom-

Table I

No. of experiment	Phenol used in grams	Bromine used in grams	Total concentration in cc.	Time	Bromine left, in grams	Bromine used up, in grams
Phenol in Glacial Acetic Acid						
1	0.05	0.2099	11	24 hrs.	0.0475	0.1624
2	0.05	0.3147	14	"	0.1366	0.1781
3	0.05	0.2801	13	"	0.1051	0.1750
4[1]	0.05	0.2365	13	1 wk.	0.0479	0.1886
Phenol in Chloroform						
1	0.05	0.1768	11	24 hrs.	0.0126	0.1642
2	0.05	0.1768	11	"	0.0084	0.1684
3	0.05	0.1768	11	"	0.0104	0.1664
4[2]	0.05	0.2231	14	1 wk.	0.0242	0.1989
Phenol in Carbon Tetrachloride						
1	0.05	0.2613	11	24 hrs.	0.0975	0.1638
2	0.05	0.3055	12	"	0.1386	0.1669
3	0.05	0.3492	13	"	0.1861	0.1631
4	0.05	0.2619	11	1 wk.	0.0870	0.1749
Phenol in Carbon Bisulphide						
1	0.05	0.1846	9	24 hrs.	0.0352	0.1494
2	0.05	0.2308	10	"	0.0931	0.1377
3	0.05	0.2805	11.08	"	0.1318	0.1487
4	0.05	0.2769	11.00	1 wk.	0.1087	0.1682

phenol. The bromine used was dissolved in chloroform. After standing for two days this mixture was poured into an evaporating dish and allowed to evaporate spontaneously. There was left an oily liquid which, when poured into water, sank to the bottom of the vessel and on cooling in ice water solidified to a white solid. This substance was found to melt at 34°. A bromine determination gave 60.15 per cent. bromine; calculated for dibromphenol, 63.49 per cent. Con-

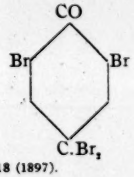
[1] In the first three of the above experiments the quantity of bromine acting on the glacial acetic acid was found to be negligible. In experiment (4), however, a correction has been made for the amount of bromine acting on the acid. Thus, in a control experiment extending over one week 0.2791 gram of bromine in 13 cc. of acetic acid took 20.6 cc. 0.1 N sodium thiosulphate, equivalent to 0.2365 gram of bromine. Hence, in experiment (4) of the above series there was left only this last amount of bromine to react with the phenol.

[2] In this experiment a correction was made for the amount of bromine acting on chloroform, after one week's exposure. This correction was determined as in the case of the acetic acid.

sidering the fact that the substance was not specially purified and that, owing to its low melting point, it proved difficult to handle, the agreement is sufficiently close to indicate that we are dealing with a dibromphenol. The substance is probably the 2,4-dibromphenol. It is evident from these observations that in its conduct toward bromine in organic solvents phenol is similar to many other simple aromatic substances. A considerable number of these are converted directly into dibrom derivatives on bromination. The process is a simple act of substitution. On the other hand the conversion of phenol into tribromphenol and tribromphenol bromide, in aqueous solution, by the action of bromine, is somewhat peculiar and anomalous. Similar changes are shown by but few organic substances. Among those which do react similarly may be mentioned aniline which, in aqueous solution, is converted into tribromaniline by the action of bromine. So far as is known at present there is no essential difference between a solution of bromine in water and in an organic solvent, beyond the fact that in all probability a portion of the bromine is hydrated in its aqueous solution.

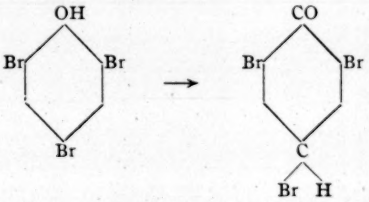
According to Jakowkin[1] bromine in its aqueous solution cannot be ionized, so that these differences in the conduct of bromine in water and organic solvents towards phenol are evidently not referable to the bromine but to the phenol.

One of us, Kastle, is inclined to the opinion that the peculiar conduct of phenol, in its aqueous solution, towards bromine is in some way dependent on the tendency of phenol to form a quinoid derivative. It is well known that in the presence of water bromine converts tribromphenol into tribromphenol bromide. This latter compound is a quinoid derivative having the constitution

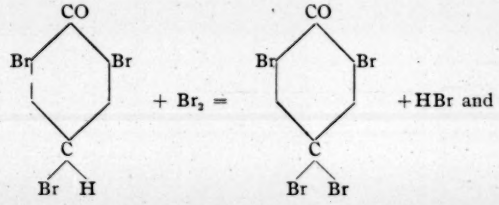


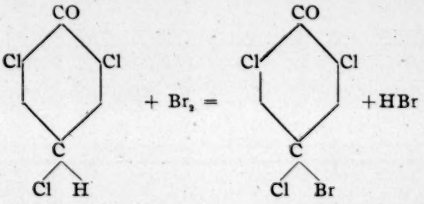
[1] Ber. d. chem. Ges., **30**, 518 (1897).

Kastle and Gilbert have shown that trichlorphenol is converted in the same way into trichlorphenol bromide on the addition of bromine to an aqueous suspension of trichlorphenol. These changes can be readily accounted for on the supposition that under the influence of water the tri-substitution products of phenol are converted into the corresponding quinoid derivatives. Thus,

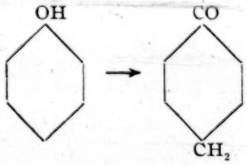


If now we have the quinoid hydrogen in this last compound replaced by bromine we have tribromphenol bromide and trichlorphenol bromide produced by simple substitution. Thus,

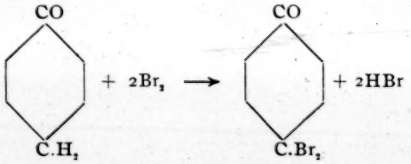




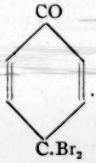
There is no reason why phenol itself might not under certain conditions pass to the quinoid form. In this event we would have



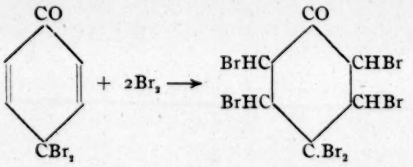
If now bromine were to replace the two quinoid hydrogens we would have



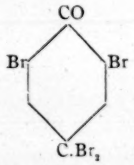
The latter compound, being a quinoid derivative, contains two double bonds, as shown by the formula



It could therefore take up two molecules of bromine thus,



By loss of hydrobromic acid this last substance would pass to tribromphenol bromide,



Kastle has lately come to believe that while tribromphenol bromide results from the action of bromine on tribromphenol, it is also the first product of the bromination of phenol in water and that the tribromphenol is formed from it only by the action of an excess of phenol. Thus we see that when bromine is added gradually to an aqueous solution of phenol a yellow precipitate is always formed which, by reaction with the excess of phenol present, becomes white. Now tribromphenol bromide is yellow, whereas tribromphenol is white. Hence it appears probable that tribromphenol bromide is formed first whenever bromine acts on an aqueous solution of phenol and that only through interaction of this substance with phenol is tribromphenol produced. On the other hand, in the absence of water and in organic solvents bromine acts upon phenol in precisely the same way that it does upon other aromatic substances. That is, the change is one of simple substitution.

UNIVERSITY OF VIRGINIA
July, 1911

A STUDY OF ORTHOAMINOPARASULPHOBENZOIC ACID AND ITS DERIVATIVES, WITH SPECIAL REFERENCE TO THEIR FLUORESCENCE

BY JOSEPH H. KASTLE AND R. L. HADEN

[SECOND COMMUNICATION]

The Esters of o-*Amino*-p-*sulphobenzoic Acid.*—As pointed out in a previous communication[1] our earlier attempts to

[1] THIS JOURNAL, **45**, 58–78.

esterify this amino acid by the action of ethyl iodide on the disilver salt of the acid invariably resulted in the production of a N-ester of the formula

$$C_6H_3\begin{cases}COOH\\NH.C_2H_5\\SO_2OH\end{cases} + H_2O$$

In one experiment, however, a very small amount of a sulphur-yellow compound crystallizing in fine needle-shaped crystals and melting at about 160° was obtained. Later it was observed that this yellow substance is soluble in ether, chloroform and alcohol. Putting to account this additional knowledge regarding its solubility in these organic solvents the attempt has been made to obtain the yellow compound in larger quantity. Six grams of the dry, finely pulverized disilver salt of the amino acid was placed in a small Erlenmeyer flask and ethyl iodide added in small portions at a time. The substances reacted almost immediately with slight rise of temperature. When the reaction was apparently complete another portion of ethyl iodide was added and the flask was tightly closed with a cork. It was then allowed to stand overnight at room temperature. The next day the excess of ethyl odide was removed by a current of air, and the residue extracted with absolute alcohol and filtered. A yellow solution was thus obtained which on the gradual addition of water became milky and gave a crop of fine, yellow, needle-shaped crystals. These were filtered off and dried in the air. The yellow compound thus obtained was found to weigh 0.9 gram and to melt at 151°–153°, uncorrected. The small yield of this compound is discouraging and difficult to explain. The fact, however, that the N-ester is always formed in this reaction renders it probable that the esterification of the disilver salt of the amino acid takes place in the following stages:

$$(1)\quad C_6H_3\begin{cases}COOAg\\NH_2\\SO_2OAg\end{cases} + C_2H_5I = C_6H_3\begin{cases}COOAg\\NH_2.C_2H_5I\\SO_2OAg\end{cases}$$

$$(2)\quad C_6H_3\begin{cases}COOAg\\NH_2C_2H_5I\\SO_2OAg\end{cases} = C_6H_3\begin{cases}COOAg\\NH.C_2H_5\\SO_2OAg\end{cases} + HI$$

(3) $C_6H_3\langle^{COOAg}_{NH.C_2H_5}_{SO_2OAg} + HI = C_6H_3\langle^{COOH}_{NHC_2H_5}_{SO_2OAg} + AgI$

(4) $2C_6H_3\langle^{COOH}_{NH.C_2H_5}_{SO_2OAg} = C_6H_3\langle^{COOH}_{NHC_2H_5}_{SO_2OH} + C_6H_3\langle^{COOAg}_{NH.C_2H_5}_{SO_3OAg}$

(5) $C_6H_3\langle^{COOAg}_{NH.C_2H_5}_{SO_2OAg} + 2C_2H_5I = C_6H_3\langle^{COOC_2H_5}_{NH.C_2H_5}_{SO_2OC_2H_5} + 2AgI$

According to this conception of the process only half of the disilver salt of the amino acid would really go to form the tri ester and the theoretical yield of the tri ester would be reduced by half. The actual yields, therefore, amounting to from 22–36.9 per cent., would not be so bad. The above conception of the process would also explain the constant production of the nitrogen rhombic ester in this reaction.

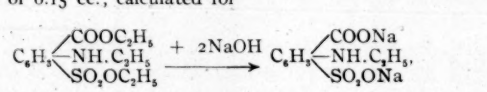
Triethyl o-Amino-p-sulphobenzoate.—The compound thus obtained by the action of ethyl iodide on the disilver salt of the amino acid is yellow and crystallizes from a mixture of water and alcohol in fine needle-shaped crystals, melting at 151°–153°, uncorrected. The compound is practically insoluble in water but soluble in a great variety of organic solvents. It contains no iodine and no water of crystallization.

On combustion by de Roode's method 0.2062 gram of the substance gave 0.1171 gram of water and 0.3918 gram of carbon dioxide; calculated for $C_6H_3\langle^{COOC_2H_5}_{NH.C_2H_5}_{SO_2OC_2H_5}$, 0.1067 gram of water and 0.3873 gram carbon dioxide. A sulphur determination by Liebig's method on 0.1070 gram substance gave 0.0742 gram $BaSO_4$, equivalent to 0.0102 gram or 9.53 per cent. sulphur; calculated for $C_6H_3\langle^{COOC_2H_5}_{NH.C_2H_5}_{SO_2OC_2H_5}$, 10.65 per cent.

This large error is probably due to the very small amount of the substance employed for analysis. The yellow substance is neutral to litmus, but its alcoholic solution is acid to

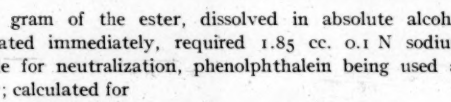
phenolphthalein and on boiling with water it also becomes strongly acid and gradually passes into solution.

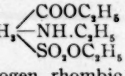
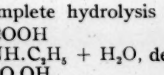
0.0925 gram of the substance boiled for eight hours with water under an inverted condenser, required 6 cc. 0.1 N sodium hydroxide for neutralization and after standing for several days the same solution required 0.15 cc. more, making a total of 6.15 cc.; calculated for



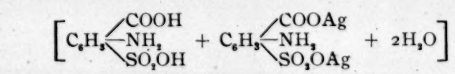
6.14 cc.

0.0562 gram of the ester, dissolved in absolute alcohol and titrated immediately, required 1.85 cc. 0.1 N sodium hydroxide for neutralization, phenolphthalein being used as indicator; calculated for



1.86 cc. It should also be borne in mind in this connection that the ease with which one of the ester groups is hydrolyzed or saponified is characteristic of the sulphonic esters. It is evident, therefore, from these results that the yellow substance resulting from the action of ethyl iodide on the disilver salt of the amino acid is a triethyl ester of the constitution  which on complete hydrolysis yields the nitrogen rhombic ester,  , described in our first communication.[1]

The Acid Silver Salt of o-*Amino* p-*sulphobenzoic Acid*,



During the course of this investigation the attempt was made

[1] THIS JOURNAL, **45**, 71–74.

to prepare a benzoyl derivative of the amino acid by treating the disilver salt of the acid with benzoyl chloride. In one experiment 6 grams of the disilver salt was heated in a sealed tube with the calculated amount of benzoyl chloride until apparently the reaction was complete. The contents of the tube were then treated with successive portions of ether and acetone to remove the excess of benzoyl chloride. The residue was then boiled with water and filtered to remove the silver chloride and the filtrate evaporated to crystallization. A quantity of prismatic crystals which were found to darken in the light was thus obtained. They gave an acid reaction to litmus and were found to contain silver.

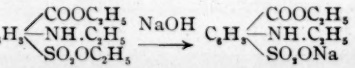
0.1335 gram of this salt required 3.8 cc. 0.1 N sodium hydroxide for neutralization; calculated for $C_6H_3\begin{cases}COOH\\NH_2\\SO_3Ag\end{cases} + H_2O$, 3.9 cc.

0.1240 gram of the salt took 3.7 cc. 0.1 N ammonium sulphocyanide; calculated according to the above formula it should have required 3.9 cc.

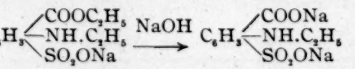
0.6770 gram of the salt, heated in the air bath at 150° for one hour, lost 0.0363 gram, or 5.36 per cent., of water of crystallization; calculated according to the above formula, 5.26 per cent.

Repeated analyses have established the composition of this acid silver salt and in harmony with these results the best way of preparing the salt consists in heating together, in water, the calculated quantity of the amino acid and the disilver salt, filtering from any undissolved disilver salt and evaporating the filtrate to crystallization. In this way large amounts of the acid silver salt have been prepared. Our earlier attempts to esterify this acid silver salt resulted in the formation of an acid substance which we now have reason to believe consisted of a mixture of the original amino acid and the nitrogen rhombic ester in varying proportions. These results were obtained before we had discovered a satisfactory method of isolating the yellow tri ester described in the foregoing. Having observed that absolute alcohol could be

employed satisfactorily in extracting the yellow tri ester from the products of the reaction of ethyl iodide on the disilver salt of the amino acid, it occurred to us that possibly it could also be employed to advantage in the isolation of the ester resulting from the action of ethyl iodide on the acid silver salt. Accordingly 1.0202 grams of the anhydrous acid silver salt was heated in a sealed tube, on a water bath, with an excess of ethyl iodide for one hour. On cooling large yellow crystals were seen suspended in the excess of ethyl iodide. The tube was then opened and the excess of ethyl iodide removed by warming the tube for a few minutes on the water bath. The contents of the tube were then extracted with hot absolute alcohol and filtered. Water was then added to the yellow alcoholic filtrate and the yellow crystals thus obtained were collected on filter paper and dried at room temperature in the air. There was thus obtained 0.1315 gram of a yellow substance identical in all respects with the yellow tri ester obtained by the action of ethyl iodide on the disilver salt of the amino acid. Thus, it was found to melt at 150°–153°, and when mixed with some of the tri ester which had been made from the disilver salt, the mixture showed the same melting point, namely, 151°–153°. For 0.0487 gram of the yellow ester prepared from the acid silver salt, when dissolved in absolute alcohol, was required 1.6 cc. 0.1 N sodium hydroxide for neutralization; calculated for



1.61 cc. After the first titration, the solution of the ester in alcohol was boiled under an inverted condenser, at intervals, for about ten hours. It became acid again and on the second titration took 1.7 cc. 0.1 N sodium hydroxide; calculated for



1.61 cc. There is no doubt, therefore, that the yellow ester

resulting from the action of ethyl iodide on the acid silver salt of the amino acid is the same as that resulting from the action of the iodide on the disilver salt. The residue left after extracting with absolute alcohol the yellow ester from the products of the reaction of ethyl iodide on the acid silver salt was then extracted with boiling water and filtered to remove the silver iodide. The aqueous extract was then evaporated to small bulk, when a mass of white crystals separated on cooling. These were collected on the filter and allowed to dry in the air at room temperature. They were found to be acid in reaction and to possess the characteristics of the original amino acid. Of this substance 0.1000 gram required for neutralization 8.75 cc. 0.1 N sodium hydroxide, while 0.1000 gram of the amino acid should require 8.85 cc. It is evident, therefore, that two substances result from the action of ethyl iodide on the acid silver salt of the amino acid, namely, the yellow tri ester of this acid and the original amino acid itself. This goes to prove, of course, that the acid silver salt is not a monohydrated single molecule such as $C_6H_3\begin{cases}COOH\\NH_2\\SO_2OAg\end{cases} + H_2O$, but a dihydrated, mixed acid salt consisting of one molecule of the amino acid and one of the disilver salt of the amino acid, having the formula

$$\left[C_6H_3\begin{cases}COOH\\NH_2\\SO_2OH\end{cases} + C_6H_3\begin{cases}COOAg\\NH_2\\SO_2OAg\end{cases} + 2H_2O\right]$$

The last formula enables us to account for the conduct of the acid silver salt on esterification with ethyl iodide. Up to the present we have obtained no evidence of the existence of such acid esters of the amino acid as the following:

$$C_6H_3\begin{cases}COOC_2H_5\\NH_2\\SO_2OH\end{cases}, \quad C_6H_3\begin{cases}COOH\\NH_2\\SO_2OC_2H_5\end{cases},$$

$$C_6H_3\begin{cases}COOC_2H_5\\NH.C_2H_5\\SO_2OH\end{cases} \text{ and } C_6H_3\begin{cases}COOH\\NH.C_2H_5\\SO_2OC_2H_5\end{cases}$$

Such compounds would be of great interest as possibly affecting the fluorescence of the parent acid and every effort will be made to prepare them. From all that is known at present, however, regarding the conduct of the amino acid on esterification we must confess that we have little hope of success. In fact, the possibility of the existence of certain of these compounds appears doubtful.

As indicated in our first communication the study of *o*-amino-*p*-sulphobenzoic acid was originally undertaken with the view of determining the influence of simple chemical changes in constitution on the degree and character of the fluorescence exhibited by the original compound. This has proven far more difficult than was originally contemplated by reason of the difficulty of obtaining even the simpler derivatives of this acid. In view, therefore, of our original purpose it seemed desirable to compare the two esters already described with the parent amino acid as to fluorescence in various solvents. These solvents were selected at random from the chemicals on hand at the time and without any particular regard to their chemical nature. The results of these observations are given in Table I.

It is evident from these observations that of the three substances here under consideration the tri ester exhibits fluorescence in by far the greatest number of different solvents. This is evidently due to the fact that this substance is soluble in a greater number of solvents than either of the other two compounds. The phenomenon of fluorescence is a phenomenon of solution, at least to a great degree, and hence if a substance is not soluble in a given solvent it does not fluoresce on being brought in contact therewith. Whether either of the substances here under consideration would fluoresce in the dry state in ultraviolet light has not as yet been determined, but it seems hardly likely that they would do so. Another point of interest in this connection is that in all strictly indifferent solvents in which the compound is soluble the tint or quality of the fluorescence is the same, whereas water and the organic acids alter the quality of the fluorescence to some extent.

It is also evident from the above comparison that the intro-

Table I

Solvent	Amino acid	Nitrogen rhomic ester	Yellow tri ester
Water	Purple fluorescence, not as pink as in methyl alcohol	Strong blue fluorescence, more blue than in organic solvents	No fluorescence
Ethyl alcohol	Slight pinkish purple fluorescence	Strong blue fluorescence	Strong blue fluorescence
Methyl alcohol	Purple fluorescence, pinkish tinge	"	Blue fluorescence, not so strong as in chloroform
Ether	No fluorescence	No fluorescence	Strong blue fluorescence
Chloroform	"	"	"
Carbon bisulphide	"	"	No fluorescence
Amyl alcohol	"	Slight blue fluorescence, deep blue on standing	Strong blue fluorescence
Glycerol	Slight pinkish purple fluorescence	Strong blue fluorescence	No fluorescence
Toluene	No fluorescence	No fluorescence	Strong blue fluorescence
Turpentine	"	"	Slight purplish blue fluorescence
Acetone	"	No fluorescence at first, strong blue on standing	Strong blue fluorescence
Pyridine	"	No fluorescence	No fluorescence, or, if any, trace of blue

Table I—(Continued)

Solvent	Amino acid	Nitrogen rhomic ester	Yellow tri ester
p-Xylene	No fluorescence	No fluorescence	Strong blue fluorescence
Cymene	"	"	"
Carbon tetrachloride	"	"	"
Glacial acetic acid	On standing, slight pinkish purple fluorescence	Strong blue fluorescence	Strong blue fluorescence, lighter blue than in chloroform
Butyric acid	No fluorescence	Slight blue fluorescence, strong on standing	Strong blue fluorescence
Methyl salicylate	"	No fluorescence	Blue fluorescence, similar to chloroform
Ethyl benzoate	"	"	Strong blue fluorescence
Ethyl acetate	"	"	Strong blue fluorescence more blue than in chloroform
Lactic acid	Slight blue fluorescence, on standing	Trace of blue fluorescence, decided on standing	Light blue fluorescence, similar to acetic acid, only not so strong
Ethylene chloride	No fluorescence	No fluorescence	Strong blue fluorescence
Ethylidene chloride	"	"	"
Ethyl bromide	"	"	"
Ethylene bromide	"	"	"
Nitrobenzene	"	"	No fluorescence
Olive oil	"	"	"
Oil of lavender	"	"	Blue fluorescence
Oil of peppermint	"	"	"

duction of an ethyl group into the compound in place of one of the acid or amino hydrogens has the effect of greatly increasing the blue tint of the fluorescence. This is seen to special advantage in the aqueous and alcoholic solutions. Thus in a mixture of equal volumes of water and alcohol the amino acid shows a pinkish purple fluorescence, the nitrogen rhombic ester pure blue and the yellow tri ester pure blue, with a yellowish solution. Since the publication of our first communication on this subject, we have noted from an examination of the literature that aminoterephthalic acid, $C_6H_3\begin{cases}COOH\\NH_2(o)\\COOH(p)\end{cases}$, is also fluorescent in aqueous solution. That such is the case has been confirmed by Mr. Lester Patton, working in this laboratory. Mr. Patton finds that in dilute aqueous and alkaline solutions aminoterephthalic acid shows a reddish blue fluorescence, whereas in acetone it shows a pure blue fluorescence. He also observed that the mono- and diethyl esters of this acid exhibit a pure blue fluorescence in their aqueous solution. So that, so far as fluorescence is concerned, aminoterephthalic acid is apparently quite analogous to *o*-amino-*p*-sulphobenzoic acid.

We hope in the near future to make a more careful investigation of aminoterephthalic acid and its derivatives with the view of comparing them, as to fluorescence, with the corresponding derivatives of the acid here under consideration and those of aminobenzene-*p*-disulphonic acid which, so far as we have been able to ascertain from the literature at present available, has never been made.

UNIVERSITY OF VIRGINIA
July, 1911

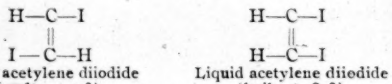
THE SYNTHESIS OF FUMARIC AND MALEIC ACIDS FROM THE ACETYLENE DIIODIDES

BY EDWARD H. KEISER AND LEROY MCMASTER

In 1890 one of us (Keiser[1]), by treating solid acetylene diiodide in alcoholic solution with potassium cyanide and

[1] THIS JOURNAL, **12**, 99.

caustic potash, succeeded in making fumaric acid. Subsequently in 1899 Keiser[1] obtained for the first time a pure liquid isomer of the solid acetylene diiodide and showed that these substances were geometrical isomers and at that time expressed the view that the solid acetylene diiodide was to be regarded as the *trans* or fumaric form and the liquid geometrical isomer the *cis* or maleic form. Their configuration was represented thus:



Solid acetylene diiodide (melts at 73°) — Liquid acetylene diiodide (boils at 185°)

We have now established these formulas by repeating and confirming the earlier work upon the synthesis of fumaric acid from the solid acetylene diiodide, and, in addition, we have transformed the liquid diiodide into maleic acid.

Synthesis of Fumaric Acid

Experiment No. 1.—Solid acetylene diiodide (4.11 grams) was dissolved in 150 cc. absolute alcohol, 3 grams of powdered potassium cyanide added and the mixture boiled on a water bath under a reflux condenser for 47 hours. Three grams of solid caustic potash were now added and the heating continued for one and one-half hours, when ammonia was no longer given off. The solution was filtered and allowed to evaporate spontaneously. A mixture of crystals was obtained, some of which were needle-shaped. Qualitative tests showed the presence of iodide, cyanide and fumarate in this mixture. The fumarate was then separated and purified as follows: The crystals were dissolved in water and silver nitrate added until a precipitate was no longer formed. The precipitate, consisting of silver fumarate and some silver iodide and cyanide, was digested with dilute ammonia and the mixture filtered. The filtrate now contained the fumarate and some cyanide. Dilute nitric acid was now added in slight excess. This caused the cyanide to be precipitated, but held the fumarate in solution. After filtration the filtrate,

[1] THIS JOURNAL, **21**, 261.

containing the fumarate, was now made exactly neutral with ammonia. A white precipitate formed. This was collected upon a filter and again dissolved in dilute nitric acid and precipitated by ammonia. The silver fumarate was then collected upon a hardened filter and dried at 100° for one and a half days. The salt turned slightly brown and when heated it deflagrated like gunpowder. Determinations of the percentage of silver gave the following results:

0.1354 gram of salt gave 0.1183 gram AgCl.

0.2050 gram of salt gave 0.1792 gram AgCl.

	Calculated for $C_4H_2O_4Ag_2$	I	II
Ag	65.43	65.74	65.78

These determinations were made by dissolving the weighed amounts of fumarate in dilute nitric acid and adding hydrochloric acid in slight excess. The silver chloride was filtered, dried and weighed. The filtrate from the silver chloride, containing the free fumaric acid, was evaporated to dryness, when a white flaky residue was obtained. This was dried at 105°. It weighed, in the first analysis, 0.0428 gram instead of 0.0476 gram, calculated. A small quantity of this residue was placed between watch glasses and heated in an air bath. At 200° it sublimed into the upper watch glass. A sample of pure fumaric acid (Kahlbaum) acted likewise. Some small crystals of this synthetic fumaric acid were introduced into a melting-point capillary and heated beside a similar specimen of the pure fumaric acid in a sulphuric acid bath. At 200° each specimen sublimed to the upper cold part of the capillaries.

Experiment No. 2.—Ten grams of solid acetylene diiodide and 7.5 grams potassium cyanide were heated with alcohol for 50 hours on the water bath under a reflux condenser. Eight grams of caustic potash were then added and the boiling continued until ammonia was no longer given off. The hot alcoholic solution was poured off and allowed to evaporate. The salt that separated was treated with dilute nitric acid and silver nitrate added. The precipitate was filtered off and the filtrate was exactly neutralized with ammonia. The white precipitate of silver fumarate was redissolved and re-

precipitated as in the first synthesis and dried at 105°–110°. It turned slightly brown on drying. A quantitative determination of silver gave this result:

0.1734 gram of salt gave 0.1516 gram AgCl.

	Calculated for $C_4H_2O_4Ag_2$	Found
Ag	65.43	65.80

The free fumaric acid was obtained by evaporating the filtrate from the silver chloride, as described above. It sublimed at 201° in the melting-point apparatus.

Synthesis of Maleic Acid

Liquid acetylene diiodide was prepared and purified by freezing as described by Keiser.[1] Ten grams of the pure liquid diiodide and 7 grams of potassium cyanide in absolute alcohol were boiled, under a reflux condenser, on the water bath for 53 hours. The mixture turned pink, then dark brown and finally black. A strong odor of isocyanide was noticed on opening the flask. Eight grams of solid caustic potash were added and the boiling continued for five hours, until the odor of ammonia had disappeared. The solution was filtered, a black residue remaining on the filter. This consisted chiefly of iodides and carbonaceous matter, but contained some maleate. The yellow filtrate was allowed to evaporate. The salts that separated were dissolved in water and the water solution evaporated in a desiccator. The solid matter thus obtained was treated with just enough dilute hydrochloric acid to decompose the small amount of carbonate present and then the solution was warmed to expel the gas. Barium hydroxide solution was now run in until the liquid was exactly neutral. On standing a short time a fine silky precipitate settled out. This precipitate was very similar in appearance and behavior to barium maleate made in the same way from pure maleic acid (Kahlbaum). The synthetic barium maleate was filtered off and washed with *cold* water until the wash water gave no test for barium, chlorine or iodine. The salt was then dried at 105° for eight

[1] This Journal, **21**, 264.

hours. A determination of barium gave 52.26 per cent. As the calculated value for barium in anhydrous barium maleate, $C_4H_2O_4Ba$, is 54.65 per cent. and in the salt with one molecule of water of crystallization, $C_4H_2O_4Ba.H_2O$, is 51 per cent., it was evident that our salt was a mixture, or rather it was not dried sufficiently to completely convert it into the anhydrous salt. We found at this stage of the work that Vorländer[1] stated that barium maleate does not lose water at 100° but begins to do so at 110° and that the water is completely driven off at 130°–135°. Another sample of the barium salt was dried at 110°–125° for 22 hours. Determinations of barium now gave the following results:

I. 0.2434 gram salt gave 0.2276 gram $BaSO_4$.
II. 0.1739 gram salt gave 0.1610 gram $BaSO_4$.
III. 0.3502 gram salt gave 0.3279 gram $BaSO_4$.

	Calculated for $C_4H_2O_4Ba$	Found I	Found II	Found III
Ba	54.65	54.98	54.45	55.04

A second synthesis of maleic acid was now made, with the same quantities of substances, and the same method as before. The barium salt was prepared and purified as described above. It is to be noted that the fumaric acid is not precipitated by barium hydroxide under the conditions under which we made barium maleate. The barium maleate in this synthesis was dried at 135° for three days. The analysis gave the following results:

0.2506 gram salt gave 0.2340 gram $BaSO_4$.

	Calculated for $C_4H_2O_4Ba$	Found
Ba	54.65	54.9

Some of this barium maleate was tested for fumarate by dissolving it in hot water to which a little nitric acid had been added, then neutralizing exactly with ammonia and adding silver nitrate. No precipitate of silver fumarate was obtained. Further, the free maleic acid from the barium salt, made in this synthesis, was prepared by dissolving the salt

[1] Ann. Chem. (Liebig), **280**, 192.

in hot water and adding sulphuric acid to the point of exact neutrality, then filtering off the barium sulphate and evaporating the filtrate. A melting-point determination of the white residue showed that it melted at 131°. Pure maleic acid (Kahlbaum) melts at 130°.

These experiments show conclusively that the solid acetylene diiodide can be converted into fumaric acid and the liquid isomer into maleic acid. This makes it highly probable that these compounds have the configuration given above, namely, that the solid diiodide has the fumaric or *trans* form, and the liquid diiodide has the maleic or *cis* form.

CHEMICAL LABORATORY
WASHINGTON UNIVERSITY
St. Louis, Mo.

THE NITRILE OF FUMARIC ACID

BY EDWARD H. KEISER AND J. J. KESSLER

In 1890 E. H. Keiser,[1] starting with solid acetylene diiodide, $C_2H_2I_2$, succeeded in making fumaric acid by means of potassium cyanide and caustic potash. Recently E. H. Keiser[2] and L. McMaster have repeated this synthesis of fumaric acid and have also made maleic acid synthetically by starting with the liquid acetylene diiodide and treating it with potassium cyanide in alcoholic solution and then boiling with alkali. In these syntheses the nitriles of the acids must be formed, in the one case the nitrile of fumaric acid and in the other that of maleic acid, and these are subsequently saponified by the alkali. Experiments made to isolate these nitriles were not successful. We have, therefore, attempted to prepare them in another way, namely, by heating fumaramide and ammonium maleate with phosphorus pentoxide. We have succeeded in making the fumaric nitrile, but have not gotten the maleic nitrile. We made the fumaramide in two ways: in the one, we started with succinic acid and made diethyl monobromsuccinate and treated this with ammonia, thus obtaining fumaramide; in the other, we

[1] THIS JOURNAL, **12**, 99.
[2] See preceding paper.

started with fumaric acid and made the dimethyl ester, which was then converted into the amide by means of ammonia. Both specimens of fumaramide were identical, and when each was heated with phosphorus pentoxide the same sublimate was obtained in each case. This sublimate we find has the composition of fumaric nitrile.

Fumaramide from Succinic Acid

Portions of 100 grams of succinic acid and 25 grams of red phosphorus were ground together in a mortar until a fine uniform mixture was obtained. This mixture was placed in a dry two-liter flask, provided with a dropping funnel and an exit tube joined to two Woulf bottles containing water to absorb the hydrobromic acid. Bromine was now dropped upon the mixture, the flask being cooled with water, and no attempt was made to hasten the action, which was quite violent at first. For each portion of 100 grams of succinic acid 454 grams of bromine were used. The reaction mixture was then allowed to stand 12 hours before distilling off the excess of bromine. This was done by disconnecting one Woulf bottle and attaching a suction pump in its place and then heating the flask on a water bath until the excess of bromine and the hydrobromic acid were driven off. This is essentially the method of brominating succinic acid recommended by Volhard[1] except that the reaction mixture was allowed to stand longer and some of the details were modified.

In one case this brominated acid was removed from the flask and weighed. The weight was found to be 300 grams. This included also the metaphosphoric acid which had been formed and which cannot be separated at this point since it is soluble in the bromsuccinyl dibromide. This bromsuccinyl dibromide fumes strongly in the air and will, if left in contact with the air, be completely decomposed. When it is allowed to stand in a closed bottle a white layer of succinic anhydride rises to the top and the heavy oily bromide becomes quite clear and may be poured off from the anhydride which forms a crust on top of the oily liquid. The amount of anhydride

[1] Volhard: Ann. Chem. (Liebig), **242**, 144.

was not greater than 5 per cent. of the total product. In one case more bromine was used but the increase in the yield of bromsuccinyl bromide was not sufficient to justify this procedure.

Without opening the flask from which the excess of bromine and hydrobromic acid have been distilled 300 grams of absolute ethyl alcohol are now added drop by drop. The hydrobromic acid given off is absorbed in water in the two Woulf bottles. Care should be taken that the alcohol enters into action as it drops into the flask. If the temperature is low this may not always be the case and a considerable excess of alcohol will accumulate. If now the flask be shaken a very violet reaction will occur and an enormous amount of hydrobromic acid will be liberated in a short time, thus making the operation a dangerous one. After all the alcohol has been added, which requires several hours, the reaction mixture is again allowed to stand overnight, then the excess of alcohol and the hydrobromic acid are removed by distillation on a water bath, a suction pump being used to diminish the pressure. Water is now added in excess to the diethyl monobromsuccinate. This dissolves the metaphosphoric acid and any excess of alcohol that may remain. After thorough shaking the water solution is poured off by decantation from the ester. This washing is repeated several times, and finally the oily ester is washed with water containing a small amount of bicarbonate of soda to remove the last traces of phosphoric and succinic acids.

To the ester is now added dilute ammonia, made by mixing 450 cc. of water with 50 cc. of concentrated ammonia. The action is allowed to go on for a week, the flask being thoroughly shaken each day. The fumaramide is formed slowly. If the mixture could be continually shaken it would, no doubt, increase the velocity of the reaction. It is best to wait until the reaction has been entirely completed and no oily ester is left. During the earlier part of the work several separations of the amide were made as it was formed from day to day, but it is difficult to remove the traces of oily ester from it. If the reaction is allowed to proceed to completion the whole may be

easily filtered and washed with water, then with alcohol and ether. The amide is not very soluble in alcohol or ether but it dissolves readily in hot water. It will be observed that until the filtration of the amide all the reactions are carried out in one flask without removing the product that is sought and it is believed that this procedure helps to increase the yield. From 100 grams of succinic acid 30–40 grams of fumaramide are obtained. The theoretical yield is 96.6 grams. This method of preparing the amide cannot be hastened by using more concentrated ammonia or by heating the mixture, as other products are then formed.

Fumaric Nitrile from Fumaramide

Five grams of perfectly dry fumaramide were mixed with 12–15 grams of phosphorus pentoxide. In order to insure a thorough mixing, the fumaramide was first thoroughly pulverized and the powdered pentoxide added to the fine powder and the whole thoroughly stirred together. As water is rapidly taken up from the air no time must be lost in placing the mixture in a crystallizing dish, covering it with a funnel and heating the dish on a sand bath to about 120°. At this temperature the reaction mixture turns black and a miniature snow storm commences in the dish and the sides of the funnel are quickly covered with a deposit of a fine needlelike sublimate. Care must be taken that the funnel does not become too hot. Cool funnels must be put on from time to time until no more sublimate is obtained. The first funnel contains the nitrile crystals in best condition. The last has a deposit which sticks to the sides of the glass and which results from the fact that the temperature has risen so high that good crystals are not obtained. The contents of the funnels are removed by tapping them over a sheet of paper, when the crystals fall out. The material that sticks to the sides may be removed by dissolving it in ether and recovered by evaporating the ether.

Fumaric nitrile has a pleasant, pungent, characteristic nitrile odor. It sublimes very easily. The needlelike crystals are extremely light and if they are inhaled while floating in the air they

prove very irritating to the mucous membranes. If a few of the needles are placed in the bottom of a test tube and heated they sublime without melting. If, however, a larger amount is used, especially material that has been obtained by the evaporation of the ethereal solution, then the substance melts at 96°. It was thought at one time that two substances were produced in this reaction, one the needlelike crystals, very volatile and subliming without melting, and another substance less volatile and melting at 96°. Further experiments showed that they are identical. The best condition for the formation of the needles is to raise the temperature of the reaction mixture rapidly. With slow heating less is formed. Starting with 5 grams of fumaramide a yield of 0.15 gram of fumaric nitrile was obtained.

The analysis gave the following results:

	Calculated for $C_2H_2(CN)_2$	Found
C	61.5	61.5
H	2.6	3.1
N	35.9	37.0–35.9

The melting point of the substance prepared from fumaramide and from succinic acid, and also of that prepared directly from fumaric acid as described below, is 96° and the boiling point is 186° (760 mm.). It sublimes readily even below 100°, and it is through this property that we have been able to isolate it, as in all cases we have used temperatures lower than the boiling point.

Fumaric nitrile is easily soluble in water, alcohol and ether. When heated with alkalis, ammonia is evolved. The solution of the substance in water gives but a very slight turbidity with silver nitrate. If, however, the solution is heated but a short time with an alkaki, and then acidified and silver nitrate added, a copious precipitate of silver cyanide is obtained. The alkali seems to completely decompose the nitrile with the formation of alkali cyanide. Attempts were made to saponify the fumaric nitrile by heating it with dilute sulphuric acid in a sealed tube and thus to obtain fumaric acid but they were not successful. The amounts of nitrile used were, however, very small.

Fumaric Nitrile from Fumaric Acid

Five grams of Kahlbaum's fumaric acid was converted into the methyl ester by dissolving the acid in 35 cc. absolute methyl alcohol, conducting a stream of dry hydrochloric acid gas into the solution and allowing it to stand overnight. When the pure crystallized ester was allowed to stand in a 30 per cent. solution of ammonia for several days, it was transformed into fumaramide.

The pure white fumaramide was filtered, dried, finely pulverized and mixed intimately with 15 grams of phosphorus pentoxide. The mixture was quickly put into dry test tubes which were then placed into long combustion tubes sealed at one end. The open ends were then sealed and the part containing the test tubes with the reaction mixture heated in a Carius furnace for 48 hours at 130°. Needlelike crystals collected in the cold ends of the tubes. These crystals contained nitrogen, melted at 96° and had all of the properties of the fumaric nitrile made from succinic acid.

CHEMICAL LABORATORY
WASHINGTON UNIVERSITY
ST. LOUIS, MO.

OBITUARY

ALBERT LADENBURG

The death of Professor Ladenburg, at Breslau, on August 15th has been announced. Professor Ladenburg was born at Manheim, July 2, 1842. Receiving his preparatory education in the schools of his native city, he matriculated at Heidelberg in 1863, where he studied under Bunsen and received his doctor's degree in 1868. He then worked for a time with Friedel at Paris and with Kekulé at Ghent. With the former he began those investigations on organic silicon compounds which have done so much in helping to establish the analogy between this element and carbon, while Kekulé's influence led him to undertake his researches on benzene compounds which resulted in the proof of the equivalence of the hydrogen atoms in benzene and that there are two pairs of hydrogen atoms arranged symmetrically with respect to each hydrogen atom in the ring. Equally important was his proof of the symmetrical constitution of mesitylene. His prism formula for benzene, although now practically universally rejected,

has been of great use in the development of chemistry in that, as early as 1868, it showed the necessity of taking into account steric considerations in the formulation of the constitution of chemical compounds. He next turned to synthetic investigations, especially in the field of alkaloids, succeeding, in 1886, in preparing the first artificial alkaloid, coniine. He was awarded the Hanbury gold medal for his services in the promotion of research in drug chemistry. When van't Hoff and LeBel advanced their theory of the asymmetric carbon atom, Ladenburg became interested in the problem of racemic compounds and has since had a large share in the development of methods for the resolution of such compounds into their active components. In the later years of his life he devoted himself chiefly to inorganic problems, such as the determination of the atomic weight of iodine, of the molecular weight of ozone, etc.

Besides the large number of experimental investigations which Ladenburg carried out or directed, he was very prolific in compilatory and editorial work. The first edition of his well-known "Vorträge über die Entwickelungsgeschichte der Chemie" appeared in 1869, when he was but 27 years old, and the book has gone through four editions. Largely in collaboration with his wife, he brought out the classical works of Pasteur, Kekulé, Wurtz and Berthelot. Under his direction, a 13-volume dictionary of chemistry was issued. Within the last three years he has published addresses on a multitude of natural phenomena, many of them extending far beyond the field of chemistry.

In 1872, Ladenburg was appointed "Professor Extraordinarius" at Heidelberg and the following year went to Kiel as professor of chemistry. From there he was called to Breslau in 1889, where he remained until forced by ill-health, in 1909, to give up active work. During his lifetime he was awarded many honors, and he was a member of numerous scientific societies.

REVIEWS

Traité Complet d'Analyse Chimique Appliquée aux Essais Industriels. Par J. Post, Professeur Honoraire à l'Université de Goettingue, et B. Neumann, Professeur à la Technische Hochschule de Darmstadt, avec la collaboration de nombreux chimistes et spécialistes. Deuxième édition française entièrement refondue. Traduite d'après la troisième édition allemande et augmentée de nombreuses additions par G. Chenu, Ingénieur E. P. C. et M. Pellet, Ingénieur I. N. A. Tome premier, quatrième fascicule. Avec 210

figures dans le texte et 36 planches hors texte, comprenant 101 photographies. Paris: Librairie Scientifique A. Hermann et Fils. 1911. pp. iv + 492. Price, Fr. 18.

The translation of this well-known treatise follows for the most part very closely the German edition, but many of the chapters have been elaborated or added to by the translators. Of the 490 pages, 236 are devoted to the subject of Metallography. The translation follows the original of P. Goerens which has been published separately as a book and of which there is a good English translation. Some new material has been added to the text which will add considerably to the value of the book, and the number of illustrations has been increased. The subject is treated extensively and includes chapters on pyrometry, preparation and use of polishing powders, microscopic technique and apparatus, the establishment of thermal equilibrium, diagrams of many binary and a few ternary alloys. Many of the diagrams are discussed in detail and illustrated with photomicrographs. The diagrams are more up-to-date than those originally used by Goerens in his book, although some of the earlier less accurate work is still retained. It is unfortunate that the diagrams are reproduced with the German wording, except in a few cases, although a glossary of terms is given at the end of the chapter. The translators have added much of value, particularly in the section treating of pyrometry.

Much of the second half of the book is devoted to the consideration of the analytical chemistry and physical properties of the acids, sulphuric, hydrochloric and nitric, and the important commercial salts of these acids.

There is an appendix of 30 pages on spectrum analysis written by A. de Gramont, of Paris, and a supplement to the first volume dealing with the analysis of coal, gas, lubricants and steel. Much of this is too briefly treated to be of value.

H. F.

New Ideas on Inorganic Chemistry. By Dr. A. Werner, Professor of Chemistry in the University of Zürich. Translated, with the author's sanction, from the second German edition by Edgar Percy Hedley, Ph.D., A.R.Sc.I., Lecturer and Demonstrator in Chemistry, University of Birmingham. London, New York, Bombay and Calcutta: Longmans, Green & Co. 1911. Pages xvi + 268.

In 1893 Werner published his first paper[1] on the constitution of inorganic compounds, which shed a flood of light upon this field and showed how many apparently unrelated facts could be correlated and harmonized. The constitution of the metal-ammonia compounds (metalammines) and of the

[1] Z. anorg. Chem., 3, 267–330 (1893).

double halides was shown to be essentially the same as that of ordinary salts with water of crystallization. The leading idea was that there are two kinds of valence. The "principal" bonds serve to hold together the metal and acid radicals in such compounds as $CaCl_2$, $FeCl_3$, etc. When anhydrous salts take up water of crystallization or are transformed into metalammines by taking up ammonia or analogous compounds, the new groups entering the molecule are held by the secondary "coordinate" bonds. Considering the elements in general, the principal valence may have any value from one to seven, and it often varies for a given element. The "coordination number" is sometimes four, but in the great majority of cases is equal to six. The groups held by the coordinate bonds are believed to be in closer proximity to the central atom than are the acid radicals. Such characteristic formulas as the following are used to indicate which groups are held by the two kinds of bonds: $[Ca(H_2O)_6]Cl_2$, $[Fe(H_2O)_6]Cl_3$, $[Co(NH_3)_6]Cl_2$, $[PtCl_6]K_2$, $[Co(NO_2)_6]K_3$, etc.

What has been said gives only a slight hint, an inkling, of the many ramifications of the theory of Werner. In every paper he has written since the one already referred to, there has been some new idea advanced or some new compounds for which vacant niches were waiting have been described. In 1905 there appeared the first addition of his book. Five years later the second, enlarged edition was published, of which the book now under review is a translation. "Werner's theory" has for so long a time been a by-word in chemistry that a translation into English ought to be of great value to students not well enough acquainted with the German language to unravel the unusually intricate sentences with which the original abounds. This intricacy justifies the translator in dividing sentences and using circumlocutions, but it does not excuse the numerous incorrect translations and misstatements in the book before us.

Among the minor faults are incorrectness and inconsistency in spelling, and grammatical errors. Two typical sentences illustrating the last point are found on page 16. "When the molecular composition of compounds * * * * are examined," and "the combining values * * * for hydrogen is variable."

Three times, on pages 4 and 6, we find "Blitz," as well as in several other places, and only once do we see "Biltz." "Rhubidium" is used three times on pages 7 and 8, as well as elsewhere, though the correct spelling is used now and then. "Paladium" occurs on pages 65 and 105. In a number of places "ammonium" is used for "ammonia," while

"ammin" and "ammine" are used indiscriminately. Mistakes like these and the more serious ones now to be mentioned are so numerous that in the translation there are only 63 out of 268 pages on which some correction has not been necessary.

Some examples of incorrect translation may be given, if for no other reason than to justify the criticisms of the reviewer.

On page 59, in discussing the change of active into inactive amyl alcohol, we read, "it even takes place during the preparations of the active form," the German wording being "bei der Darstellung des Alkoholates." In the next sentence we learn that "heat transforms active lactic acid into the inactive form," although Werner wrote "gewöhnliches Lactid." Two lines further on we read "when aspartic acid is heated to 170–180° with any salt of hydrochloric acid." The German is "aktive Asparaginsäure, als salzsaures Salz mit Wasser auf 170 bis 180° erhitzt."

By the translator's apparent forgetfulness of the old terms "carburet" and "hydruret" he entirely misses the point of the first two sentences on "Nomenclature" (page 74) in which Werner advises the use of the ending "-ide" in place of "-ür." He gives as examples of the usage to be avoided the names "Hydrür" and "Carbür." These are unfortunately translated "hydride" and "carbide."

On page 81, near the bottom, we read "different hydrates (acids) and salts may be derived from the same acidic anhydride of an oxide." This is hardly an intelligible translation of "leiten sich von gewissen als Säureanhydride wirkenden Oxyden verschiedene Hydrate (Säuren) und Salze ab."

The words (page 85) "polyhalides, *i. e.*, compounds the positive radical of which consists of several halogen atoms" give no very clear idea of "Verbindungen, die auf eine Valenz der positiven Radikale nicht nur ein, sondern mehrere Halogenatome enthalten."

On page 198 we read "This idea explains the enormous increase in electrical conductivity which water undergoes on the solution of ammonia." Werner wrote "Auf Grund dieser Anschauung wird das abnorme elektrochemische Verhalten des Ammoniaks in wässeriger Lösung, welches in der geringen Leitfähigkeit desselben zum Ausdruck kommt, verständlich."

Page 236: "Isomeric with the metaphosphates is a series of salts in which four of the six metals are replaceable." which is too free a translation of "Isomer mit den Metaphosphaten ist eine Salzreihe in der auf sechs Metaphosphatreste vier substituierbare einwertige Metallatome kommen."

Many more examples of this sort might be given but enough has been said to show that the book was translated and published in too great a hurry. Werner has written with such evident care and precision that it is a pity that the translation should contain so many passages often utterly misleading, which, when they may not be ascribed to carelessness, are apparently due to a misapprehension of the meaning of the original.

We do not wish to condemn the book utterly, for in spite of its many faults, which it will be possible to correct in a future edition, it is the only source of information regarding Werner's ideas for those who read German with difficulty, or not at all.

C. E. WATERS.

KAPILLARCHEMIE. Eine Darstellung der Chemie der Kolloide und verwandter Gebiete. Von DR. HERBERT FREUNDLICH, Privatdozent an der Universität Leipzig. Leipzig: Akademische Verlagsgesellschaft m. b. H. 1909. S. viii + 591. Preis; brosch., M. 16.50; geb., M. 17.50.

This volume gives a well-balanced treatment of the entire field of capillary chemistry. Its contents fall under three divisions: A. The general properties and deportment of surfaces of separation. B. Disperse systems. C. The technical and physiological significance of capillary chemistry. The first two divisions comprise the main substance of the work, to the last but eight pages are devoted. An appendix gives in tabular form the methods of preparation and the properties of sols in both aqueous and nonaqueous media.

Under the first division the several surfaces formed by the phase pairs liquid—gas, solid—gas, liquid—liquid and solid—liquid are treated of in detail. Chapters are devoted to capillary electrical phenomena and to the thickness, stability and other properties of the surface film.

Following Wo. Ostwald, the author describes as disperse systems those in which the surfaces of contact between the phases concerned are of very great area. In this division also the systems are classified according to the general physical nature of the phases that are in contact. The properties of clouds, smokes and foams are here briefly but adequately treated, while over 200 pages are given to a clear and most interesting discussion of the more broadly significant sols and gels.

A brief outline is all that is attempted of the technical bearings of the subject. Its importance in such processes as dyeing, tanning and photography, and in bacteriology, is pointed out.

A central conception of the book, that of adsorption, is introduced early, and is largely used as a unifying principle. The approximate adsorption law, due primarily to Gibbs, and elaborated by Milner, is expressed by the equation

$$u = -c/RT(\partial\sigma/\partial c)$$

σ being the surface tension of a solution, c the concentration and u the excess in concentration, per unit surface, in the surface layer. From this law and the empirical relation

$$\sigma_1 - \sigma_2 = sc^{\frac{1}{n}}$$

σ_1 and σ_2 being the tensions of solvent and of solution and s and $\frac{1}{n}$ being constants, the relation

$$u = \alpha c^{\frac{1}{n}}$$

is gained, and in its several forms is shown to have a remarkably broad application. This is brought out in an especially satisfactory manner in the case of the adsorption of gases by solids.

To write comprehensively and clearly on a subject of great complexity and that is undergoing unusually rapid development is a difficult task. This the author has performed with signal success. The book is one that calls for, but richly repays, careful reading; it is an excellent treatment, by a foremost worker, of a subject of general interest. GEO. H. BURROWS.

THE CHEMISTRY OF THE COAL-TAR DYES. By IRVING W. FAY, PH.D. (Berlin), Professor of Chemistry, Polytechnic Institute, Brooklyn, N. Y. New York: D. Van Nostrand Company. 1911. pp. vi + 467. Price, $4.

This book is intended for students and dyers who have a good knowledge of general chemistry and some knowledge of organic chemistry. After several introductory chapters dealing with the chemistry of the benzene series as related to dyestuffs, the author takes up in eleven chapters the chemistry of the various groups of dyestuffs and of a number of the dyes. Chapters on the seven colors allowed in food in this country and on mordants are also included, and there is a chapter containing 44 laboratory experiments for the preparation of various dyes or materials used in their manufacture. Diagrams and formulas are used skillfully to bring out complex chemical relations. Students and others who desire a knowledge of the chemistry of dyestuffs will find this book very useful.

G. S. F.

DIE KONSTITUTION DER CHINAALKALOIDE. Von PROF. DR. EZIO COMANDUCCI, Neapel. Deutsche Ausgabe durchgesehen von DR. W. ROTH (Cöthen). Mit 5 Texttafeln. Sammlung chemischer und chemisch-technischer Vorträge, begründet von F. B. AHRENS, herausgegeben von PROF. DR. W. HERZ, Breslau. XVI Band, 4/7 Heft. Stuttgart: Verlag von Ferdinand Enke. 1911. pp. 141–306.

The monograph is a supplemented translation of Comanducci's article on the subject published in the Nuova Enciclopedia di Chimica by I. Guareschi, Vol. 6, pp. 430–505. It contains an exhaustive discussion of those of the forty, more or less, Cinchona alkaloids, the constitution of which has been established with considerable certainty. The book consists of two parts: A short general introduction of 37 pages, and a special part of 127 pages. In the first part the experimental data are arranged with a view to clearly demonstrate the presence of certain nuclei, groups and linkings in the crystallized Cinchona alkaloids, regardless of the historical sequence in which these data were obtained. In the second part the subject is treated historically, the alkaloids being taken up one by one and the gradual accumulation of evidence upon which is based the generally accepted constitution of these alkaloids being discussed. A very useful feature of the book is the arrangement of the numerous transformation products of the alkaloids into five tables in a way to show at a glance their genetic relations. From the point of view of workmanship the book is excellently gotten up. For those interested in alkaloidal chemistry it will prove of great value, as it brings together into a comparatively small volume all the results and the whole literature on one of the most important groups of natural bases. As a reference work the book could be made still more valuable by supplying it with a good index or at least a table of contents. The book is also in need of a list of errata, of which there are quite a number, though as a rule they are not very important. To mention only a few of these: On page 67, top line, the ethyl ether of apocinchene is called the ethyl ester of apocinchene; further down on the same page, line 24, from the bottom, *p*-oxycinchene ought to be replaced by *p*-oxyapocinchene; still further on the same page, line 8 from the bottom, there ought to be "an einem der zwei Kohlenstoffatomen," instead of "an diesen zwei Kohlenstoffatomen;" on page 180 the formulas of hydrobromcinchonine and hydrochlorcinchonine are wrong; the same is true of the formula of chinchonine hydrobromide on page 183, in the paragraph on tautocinchonine. A much more serious error is to be found in the opening sentences on page 178, where it is stated that "cinchonine and cinchonidine yield one and the

same desoxycinchonine." As desoxycinchonine melts at 90–92°, while desoxycinchonidine melts at 61°, the above statement is evidently an error. In fact the nonidentity of the two desoxy bases, in connection with the assumption (based upon the identity of the cinchene obtained from cinchonine with the cinchene obtained from cinchonidine) that the isomerism of cinchonine and cinchonidine is due solely to the asymmetric carbon atom to which is linked the OH group, is used by Miller and Rohde as evidence of the hydroxyl belonging to a tertiary alcohol group, since a secondary CH.OH group would become by reduction a CH_2 group, and the asymmetry of the carbon atom would be destroyed. The book is completely up-to-date, and should be in every well equipped library.

H. M. GORDIN.